Population and disease modelling in the Tasmanian devil

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Preface & Declaration by Author

This thesis contains no material which has been accepted for a degree or diploma by the University of Tasmania or any other institution, and to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due acknowledgment is made in the text of this thesis.

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Statement of Co-Authorship

Publications produced as part of this thesis:

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The following people and institutions contributed to the publication of research undertaken as part of this thesis:

Nicholas Beeton: Contributed to ideas and study design, carried out analysis and wrote the manuscripts.

Hamish McCallum, Larry Forbes and **Clare Hawkins:** Contributed to ideas and study design, assisted with analysis and edited the manuscripts.

Save the Tasmanian Devil Program: Coordinated and undertook the field collection of much of the data utilised within the manuscripts.

We, the undersigned agree with the above stated "proportion of work undertaken" for each of the above published (or submitted) peer-reviewed manuscripts contributing to this thesis.

Hamish McCallum	Elissa Cameron
(Candidate's supervisor)	(Head of School)

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General Abstract

"Therefore, since brevity is the soul of wit,
And tediousness the limbs and outward flourishes,
I will be brief…"

- William Shakespeare,* Hamlet*, Act II, sc. ii

Infectious disease threatens many wildlife populations, but managing disease in free ranging populations is difficult. Resources, including time, are almost always limited; both for collecting data, and for being able to make effective decisions using these data. Modelling is an increasingly important and widespread tool in the arsenal of the wildlife ecologist, and particularly in dealing with threatened species. It represents a low-cost method for extrapolating empirical findings to a wider context which can often be performed quickly, as compared to experimentation which can take up valuable resources or may be ethically controversial. Predictive modelling is a vital part of an adaptive management strategy, both taking from and feeding into the process of active management and passive experimentation to help enable timely and effective conservation in challenging circumstances.

This study examined the case of the Tasmanian devil (*Sarcophilus harrisii)* and its disease, known as Devil Facial Tumour Disease (DFTD), from a modelling perspective. The devil provides a classic example of a threatened species for which conservation is urgent and the consequences of the threat are potentially devastating to both its survival and the health of the wider ecosystem. In such a scenario, effective allocation of resources into the management strategies with the best chance of success is vital.

Modelling was undertaken in two sections, the first studying population dynamics on a local, closed-population scale and the second looking at spatial dynamics across the devil's range, namely the main island of Tasmania. First, a compartmental ODE model was developed and then mathematically analysed in detail using a Dynamical Systems approach. The steady states of the system were calculated and their stability analysed. Mathematical descriptions of the bifurcation points between these steady states were found based on the bifurcation parameter ρ, the measure of removal rate. The model was also studied in relation to an unfolding parameter k, the measure of the disease latent period. The model's behaviour was found to be biologically reasonable. Findings indicated the removal effort theoretically required for successful disease suppression, as well as the range of values for latent period whereby host extinction would not occur, given model assumptions. These values appeared not to be realistic for devils, suggesting that as modelled, DFTD is capable of threatening the Tasmanian devil with extinction.

A suite of compartmental models based on this work was then developed and used to analyse the disease suppression strategy that had been trialled on the Forestier Peninsula in Tasmania's south-east. Predictions from the model demonstrated that removal of infected animals, while more successful in suppressing disease when performed regularly, was unlikely to be effective in the long term under current practical constraints.

The second section of the study began with the use of statistical modelling techniques such as Boosted Regression Trees and Monte Carlo analysis to estimate the mean abundance of the Tasmanian devil prior to the emergence of DFTD. From this

analysis, a map of devil abundance across Tasmania and the first published estimate of overall pre-disease abundance were generated. The estimate was significantly lower than previous informal estimates.

This information was then used to generate a spatial model of host-disease dynamics using a reaction-diffusion model. A Bayesian Markov Chain Monte Carlo (MCMC) analysis was run on longitudinal data from populations where data were collected both before and during disease to estimate the value of model parameters at each site, and thus determine which parameters are likely to be spatially heterogeneous. The reaction-diffusion model was then fitted to data in order to provide an estimate of the pattern of the disease's spread. Though results using only trapping or only spotlighting data were unrealistic, results incorporating both datasets together looked more reasonable. No conclusive evidence was shown to point to the location of the disease origin, which remains an open question. The addition of abundance and prevalence data from different sites in future work may help the model to better fit the true pattern of disease spread.

This study has demonstrated, using both novel and established techniques, that effective and informative modelling is possible using limited or disparate data, by applying these methods to the case of the Tasmanian devil and DFTD. These techniques and future work will hopefully aid in conservation efforts for this and other species.

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Chapter 1: General Introduction

“I’m pleased to meet you,
hope you guessed my name.”

- *The Rolling Stones,* Sympathy for the Devil

Modelling wildlife diseases

Infectious disease has long been a part of life. Despite a vast improvement in humanity's understanding of how infectious diseases work and how to deal with them, numerous open questions remain. To attempt to answer these questions, an enormous multi-disciplinary literature exists at the forefront of our knowledge. Not only is there much more to learn about diseases that directly affect humans, but wildlife disease research has emerged as a distinct field in its own right. In both human and non-human populations, the issue of new and emerging diseases has demanded particular attention – for humans, these diseases have in many cases threatened mass casualties; and for wildlife populations, extinction.

It was not until the Age of Reason and the continuing toll of smallpox on 18th Century Europe that the first epidemiological model of an infectious disease was written by mathematician Daniel Bernoulli (Bernoulli 1766; reviewed in Bernoulli and Blower 2004). At the time, the only effective treatment against smallpox was variolation – purposefully infecting a person with a less dangerous strain of smallpox to induce immunity against the disease. This was a potentially dangerous treatment, with Bernoulli estimating that it would kill 0.5% of those inoculated. Using a simple mathematical analysis, he showed that the benefits of variolation far outweighed the risks both on an individual and population level. This study helped to turn the tide of the raging debate over inoculation against smallpox, eventually leading to its widespread use. Thanks to variolation and later developments, smallpox was no longer endemic in England by the end of the 19th century, and was declared globally eradicated by the World Health Assembly in 1980 (World Health Organisation, Resolution WHA 33.3) .

The subsequent development of the field of epidemiological modelling has since occurred largely in the 20th century, beginning with the work of Hamer (1906), Ross (1911), and the key results of Kermack and McKendrick (1927) (discussed in Choisy, Guégan and Rohani 2007). These works have helped to provide the theoretical basis for a vast literature of human infectious diseases (e.g. Nokes and Anderson 1988; Anderson and May 1991; Funk, Salathe and Jansen 2010). This literature has been brought to bear on high-profile diseases affecting humans in recent times: for example, Lipsitch et al. (2003) used mathematical models of SARS transmission to estimate the basic reproduction number R_0 at around 3, suggesting that public health efforts should have a substantial impact on reducing the epidemic. Specific strategies for mitigating future influenza pandemics have also been critically assessed using mathematical models, suggesting a general approach that can be used in the case of an emerging pandemic well before extensive data has been collected (Ferguson 2006). Modern modelling techniques have also been used retrospectively to examine historical epidemics from the available data, such as the Black Death and bubonic plague epidemics (Christakos, Olea and Yu 2007).

Epidemiological data regarding wildlife populations are generally far more difficult to obtain than for human populations, as self-reporting tools are not available when dealing with animals. A number of sophisticated additional techniques has been developed or appropriated from other fields in order to collect and interpret the relevant data needed for epidemiological study. Among the most important of these is the development of mark-recapture analysis, allowing epidemiologists to make robust population estimates. Though the first uses of mark-recapture date back to Petersen

(1896) and Lincoln (1930), most of the work in this field has occurred within the last 30 years (Chao 1987; Lebreton et al. 1992; White and Burnham 1999). Additional tools have also become available in recent times to study spatial ecology (e.g. GPS collars: Rempel, Rodgers and Abraham 1995) and social behaviour (e.g. proximity loggers: Hamede, McCallum and Jones 2008).

Partially as a result of the additional work required, the study of epidemiology of wildlife diseases (or epizoology) as a separate field has taken longer to emerge than has its human equivalent. Mathematical modelling of infectious diseases in nonhuman populations – both wildlife (Anderson and May 1979; May and Anderson 1979) and domestic (Cleaveland, Laurenson and Taylor 2001) – has only begun in earnest within the last 30 years or so. Since then, wildlife epidemiology has grown into an important tool for wildlife conservation efforts (Lafferty and Gerber 2002), and as an important interface with human epidemiology for studying the effects of animal diseases on human health (Daszak, Cunningham and Hyatt 2000).

Disease-related extinction mechanisms

Unlike human diseases – which, as yet, have not threatened the extinction of humanity as a species – diseases in wildlife populations are in some cases capable of causing species extinction, either on their own or in combination with other causative factors. An important consideration when modelling wildlife diseases in particular is that the host population size naturally fluctuates (Heesterbeek and Roberts 1995) both temporally and spatially. This can become particularly important when the level of disease transmission varies with population density, or when population size becomes dangerously low.

Historically, it has been widely assumed that wildlife diseases are transmitted via a density dependent, or "mass action", process (McCallum, Barlow and Hone 2001). Density dependence assumes that susceptible and infectious animals mix completely and move randomly within a closed population. This means that in a given area, the number of times each susceptible animal encounters an infectious animal will be, on average, proportional to the number of infectious animals, or *I*, in that area. If, for example, a susceptible animal has *n* interactions with infectious animals, and the probability of infection in a single interaction is *p*, then the total probability of being infected at least once is

$$1 - (1 - p)^n$$

which, where *p* is sufficiently small, is approximately equal to *np*. This in turn means that if we have *S* susceptible animals, we expect on average that *npS* animals will be infected in a sufficiently small time interval. As *n* is assumed to be a constant proportion of *I*, and *p* is assumed to be constant, we define a constant transmission coefficient

$$\beta = p\, n / I\ .$$

The rate of infection at any given time will then have the form βSI, where β is the transmission coefficient and *S* is the number of susceptible animals. If we also assume that infectious animals are being removed from the population, either by death or external processes, at a proportional rate of *d* per unit time, then

$$\mathrm{d}I/\mathrm{d}t = (\beta S - d)I$$

In this system, the number of infectious animals can only increase when $S > d/\beta$. In particular, in a naïve population where I is small and thus N is approximately equal to S, the disease can only spread above a population threshold N_T where

$N_T = d/\beta$.

As a result, density dependent diseases cannot generally cause the extinction of their host population without the additional effect of other factors. Modelling combined with epidemic data has shown that phocine distemper in the harbour seal *Phoca vitulina*, for example, can not persist below a critical community size (Swinton et al. 1998).

Recent studies have shown that some host-pathogen systems do not behave according to the assumptions made by density dependent transmission (McCallum, Barlow and Hone 2001). Many diseases are instead more closely modelled by a frequency dependent process, the most classic example being sexually transmitted diseases (May and Anderson 1987). For example, cowpox in bank voles *Clethrionomys glareolus* was shown to be better modelled by frequency dependent, or "true mass action", transmission than density dependent transmission by comparisons with field data (Begon et al. 1998).

In a frequency dependent transmission process, it is assumed that each susceptible animal has a constant number of interactions with other animals independent of the local density of the population, as would be more likely to occur in a sexually transmitted disease. The probability of it becoming infected is then approximately proportional to the probability that each interaction is with an infected animal, so I/N.

This means that the rate of infection is of the form $\beta SI/N$. In this case, again assuming a constant mortality rate d,

$$dI/dt = \beta SI/N - dI$$

so where $N \approx S$,

$$dI/dt \approx (\beta - d)I$$

and remains positive where $\beta > d$ and $I > 0$. No population threshold therefore exists for a sufficiently infectious frequency dependent disease, meaning that such diseases are capable of driving a population to extinction (Alexander and Antonovics 1988; Thrall, Antonovics and Hall 1993).

In other diseases, a combination of frequency and density dependent transmission can occur. For example, in the two-spot ladybird *Adalia bipunctata*, though the male mates promiscuously, a proportion of the females in the population limit the number of males they mate with (Webberley et al. 2002). This means that the sexually transmitted mite *Coccipolipus hippodamiae* found in this species may be transmitted by a combination of both frequency and density dependence (Ryder et al. 2005). In such a disease, intermediate behaviour arises and disease dynamics – in particular, the potential for population extinction – depend on the transmission coefficients of both modes of infection (Ryder et al. 2007).

To demonstrate, consider a disease where there are two separate modes of transmission; and where β_1 is the transmission coefficient of the density dependent

mode, and β_2 the frequency dependent transmission coefficient. The disease can be modelled by:

$$dI/dt = \beta_1 SI + \beta_2 SI/N - dI$$

$$= (\beta_1 S + \beta_2 S/N - d)I$$

so where $N \approx S$ and $I > 0$ as above, for a disease outbreak to occur in a naïve population, dI/dt must be greater than 0, giving the condition

$$\beta_1 S + \beta_2 - d > 0,$$

and so $$\beta_1 S + \beta_2 > d$$

or $$S > (d - \beta_2) / \beta_1$$

As in the purely frequency dependent case, the frequency dependent transmission rate β_2 must be greater than d for the disease to persist for very small S. Even where β_2 does not satisfy this criterion, its effect in combination with a large density dependent transmission rate (β_1) can mean that the disease can persist at a low population level without directly causing extinction. This means that a disease with only partial frequency dependent transmission is still capable of causing extinction in a wild population if the frequency dependent mode of the disease is sufficiently infectious relative to disease-induced mortality, and is capable of suppressing the population in the long term if either or both modes are sufficiently infectious.

Even where disease by itself does not bring a population to extinction, threatened species face an array of additional dangers where population levels have been suppressed by disease. Conversely, the lower a population becomes, the more likely that other processes will contribute to its extinction should numbers remain suppressed by disease (Smith, Acevedo-Whitehouse and Pedersen 2009).

It has been observed that for many species, an insufficient number of individuals aggregated in a given place can cause them some disadvantages in fitness, increasing their likelihood of extinction (Stephens, Sutherland & Freckleton 1999). The Allee effect (Allee et al. 1949) is thus defined as a positive relationship between any component of individual fitness and either numbers or density of conspecifics. The Allee effect may only manifest at an individual level, but can affect total fitness (*demographic Allee effect* - see Stephens, Sutherland & Freckleton 1999) with the effect that total fitness – and, by extension, the potential growth rate of the population – actually decreases with a decreasing population. If this decrease in fitness is sufficiently strong, any population below a certain population threshold *C* will on average tend to decrease further. This is known as a *strong Allee effect* and means that a population that is forced below *C* is likely to become extinct. In general, relatively few cases have been proven to exhibit demographic Allee effects (Gregory et al. 2010), though evidence of the existence of this critical density in a number of species is provided in Kramer et al. (2009).

There may be a number of separate reasons for this disadvantage, each having its own particular effect on individual fitness. Courchamp, Clutton-Brock and Grenfell (1999) separate Allee effects into three broad categories: genetic inbreeding leading to a loss of fitness, demographic stochasticity, and reduction in cooperative interactions when there are fewer individuals.

Genetic effects

Genetic effects, including those encompassed by Allee effects, can play an important part in infectious diseases, and especially in host-parasite interactions. Adaptation in the host or its parasite, or the loss of potential for adaptation in the host caused by the disease, can affect the likelihood of a species becoming extinct.

Infectious diseases can impact on a species' genetic diversity by a number of mechanisms. One of these is genetic drift, defined as the effect of random changes in allele frequencies (Masel 2011). This effect is more pronounced in small populations, such as those suppressed by an infectious disease. Genetic bottlenecks (Nei, Maruyama and Chakraborty 1975) and founder effects are the result of a population recovering from a very small population size. This effect can be instigated by an infectious disease; and alternatively, a population which has already undergone a genetic bottleneck in its past may be made more susceptible to infectious disease in its future by a lack of genetic diversity.

There is a long-standing controversy over the extent to which a lack of genetic diversity affects breeding success and predisposition to disease, and by extension, how much it adds to any potential extinction risk. The primary case study for this is the African cheetah *Acinonyx jubatus*, which is threatened by habitat loss among other factors. It has been argued that a lack of genetic diversity, believed to be the result of an historical population bottleneck (Merola 1994), could contribute to driving the cheetah to extinction (O'Brien 1994). In particular, a study by Crooks, Sanajayan and Doak (1998) suggests that it may be more important to survival relative to other factors, such as cub predation, than previously assumed. However, others have cast doubt on this, suggesting that the loss of fitness in cheetah populations is limited to

captive populations (Merola 1994). The debate continues, with recent publications raising doubts as to whether the cheetah's lack of diversity causes increased disease vulnerability (Castro-Prieto, Wachter and Sommer 2011) or affects the cheetah's reproductive success in captivity (May 1995; Wachter et al. 2011). Though much uncertainty remains for many of these questions, other evidence such as the documented success of "genetic rescue" in the Florida panther (Pimm, Dollar and Bass 2006) suggests that genetic diversity can be important and should be taken into account despite this uncertainty.

Demographic and environmental stochasticity

Demographic stochasticity can affect any animal species with low population abundance, particularly with fluctuating or unequal proportions of males and females. Though the median life expectancy for a species may be well-known and well-defined, the life span will usually vary substantially from animal to animal. Similarly, fecundity in a species which breeds seasonally will vary both from female to female, and between seasons. The combined effects of randomness in all of these stochastic processes can mean that if the population size is already small, there is a possibility that demographic stochasticity will cause a significant decline – or potentially extinction (e.g. passerines introduced to New Zealand; Legendre et al. 1999) – in a population that would otherwise be expected to increase or remain stable. Environmental stochasticity, on the other hand, describes random fluctuations in birth and death rates on a population scale based on environmental effects such as weather, disease and predation that are external to the population. Again, the effects of this are most pronounced on small populations. For example, the random occurrence of unfavourable environmental conditions, combined with demographic fluctuations,

may increase mortality and thereby accelerate extinction in populations of the great tit *Parus major* in the United Kingdom (Saether et al. 1998).

Cooperative interaction

The failure of cooperative interaction at low densities can occur for a range of different animal behaviours. An important example is the case of animals having difficulty finding mates at low densities, as has been observed with wolves *Canis lupus* in the Greater Yellowstone Ecosystem (Hurford, Hebblewhite and Lewis 2006). In the case of plants, small or isolated populations may not receive enough pollination to replace themselves, as is the case with the annual herb *Clarkia concinna* (Groom 1998). Another example has been observed in which anti-predator strategies become less effective at low densities. This may be happening with threatened populations of woodland caribou *Rangifer tarandus caribou* as predation still appears to occur at very low caribou density, suggesting a lack of refuge effect at low numbers (Wittmer, Sinclair and McLellan 2005). Overall, individual behaviour can change dramatically when a species is reduced to low numbers - the Vancouver Island marmot *Marmota vancouverensis* has been shown to become far less socially active at lower numbers, as well as experiencing decreased population growth (Brashares, Werner and Sinclare 2010).

Extinction risk of emerging infectious diseases

Morse (1995) defines an emerging infectious disease as either *a disease having appeared in a population for the first time* or *an existing disease, rapidly increasing in prevalence or geographic range.* Within this broad definition, there are a range of

mechanisms by which infectious diseases emerge in wildlife populations. Williams (2002) describes three categories of factors driving emergence:

a) *ecosystem alterations of anthropogenic or natural origin,*
b) *movement of pathogens or vectors, via human or natural agency, or*
c) *changes in microbes or in the ability to recognise emerging pathogens due to advances in the techniques of epidemiology.*

In earlier epidemiological studies, it was believed that only emerging infectious diseases which do little harm may be sustained by their host animal populations over the long term (Gulland 1995) except where human interference causes an imbalance. For example, rinderpest was inadvertently introduced to Africa in the late 19th century by colonising Europeans, threatening wild ungulate populations (Plowright 1982) and killing vast numbers of domestic cattle in many African countries (Tambi et al. 1999). Alternatively, disease has on many occasions been introduced intentionally in order to harm pest animal populations, such as the use of myxomatosis and rabbit calicivirus against European rabbits (*Oryctolagus cuniculus*) in Australia (Williams et al. 2002).

This assumption is increasingly being challenged in recent times, with a number of emerging infectious diseases posing an extinction risk for animal species. The amphibian chytrid fungus *Batrachochytrium dendrobatidis* is affecting frog species across the eastern seaboard of Australia (Murray et al. 2011) and, despite a long period of co-existence, is still associated with a substantial reduction of individual survival in threatened frog species, potentially causing an extinction risk (Murray et al. 2009). The Tasmanian devil *Sarcophilus harrisii* is also being threatened by an infectious disease, Devil Facial Tumour Disease (henceforth DFTD). The disease has

also in this case remained at high prevalence despite a long period of co-existence in some areas (McCallum et al. 2009). DFTD is being treated as an extinction risk, with the Tasmanian devil being declared endangered by the Threatened Species Protection Act 1995 (Tasmania), the Environment Protection and Biodiversity Conservation Act 1999 (Australia) and the IUCN Red List (IUCN 2001).

The potential threat of emerging infectious diseases, to both humans and wildlife, is often due to their ability to infect multiple species. In particular, the existence of reservoir hosts can create an extinction risk, as the existence of an abundant second susceptible species can mean that even in diseases with density dependent transmission (McCallum, Barlow and Hone 2001) there no longer exists a population threshold below which disease is not self-sustaining. For example, Ethiopian wolves *Canis simensis* are threatened by rabies because domestic dogs act as a reservoir host for the disease (Randall et al. 2006).

Ecosystem alterations can change the abundance of species that can form a reservoir host. For example, transmission of Lyme disease has been inadvertently increased by reforestation of the north-eastern USA – this has increased the populations of white-tailed deer and other animal host species (Brown and Burgess 2001). These species, in turn, act as a reservoir of the disease for humans and domestic animals.

Pathogen movement by natural agency may be caused wholly or in part by changing distributions of reservoir hosts. It is currently hypothesised that the amphibian chytrid fungus, previously mentioned as an extinction threat, was first introduced to Australia at a port in Brisbane. Since its introduction, it has spread to occupy its current range.

The disease's spread among declining species may be facilitated by the tadpoles and adults of other species acting as avirulent disease reservoirs (Woodhams and Alford 2005).

*The Tasmanian devil (*Sarcophilus harrisii*) and Devil Facial Tumour Disease*

A recent example of a disease with a major population impact is Devil Facial Tumour disease, affecting the Tasmanian devil *Sarcophilus harrisii*. The Tasmanian devil is a carnivorous marsupial – the largest extant after the demise of the Tasmanian tiger (*Thylacinus cynocephalus*). Its current range spans the mainland of Tasmania though it was once present on the Australian mainland, and has been estimated to have become extinct there around 430 years ago (Archer and Baynes 1972; Dawson 1982), potentially due to either the introduction of dingoes or increased hunting pressure (Johnson and Wroe 2003). Due to its range and status, it is one of Tasmania's top predators. An increasing body of evidence is pointing to predation as an important factor in shaping ecosystem communities (Sih et al. 1985; Chase et al. 2002). It is thus believed that the devil could potentially be a keystone species in that any changes in its distribution or abundance may have far-reaching implications on the wider ecosystem (Ritchie and Johnson 2009; Hollings et al., unpublished data). These implications may not be straightforward to determine - food webs (Pimm, Lawton and Cohen 1991) are often far more complex than they first appear (Polis and Strong, 1996) and indirect effects can play an important role in stabilising multi-species assemblages (Wootton 1994).

Devils with unusually large facial tumours were reported at Mt William National Park in the north east of Tasmania in 1996 (Hawkins et al. 2006). By 2001, there was a growing body of evidence that similar disease signs were present across a large part of the wild Tasmanian devil population, and a research effort to gather data on the mysterious disease began in earnest in 2003. Pearse and Swift (2006) established that these malignant tumours were in fact infective, and that this emerging Devil Facial Tumour Disease (or DFTD) was actually an infectious cancer. The fact that devils commonly bite each other, both during agonistic interactions and during mating (Hamede, McCallum and Jones 2008), allows the disease to spread directly via implantation of tumour cells. This cell grafting, or allograft, method of disease spread is distinct from other, more common modes of transmission such as viral or bacterial infection.

Despite public concern that DFTD was caused by anthropogenic factors – for example, the use of chemicals such as 1080 on the natural landscape – no evidence exists to support this assertion, which, in the rubric from Williams (2002) mentioned earlier, would have placed DFTD in category a): *ecosystem alterations of anthropogenic or natural origin.* It is instead now believed that the emergence of DFTD was the result of a mutation in a non-infectious cancer causing it to become infectious (Siddle et al. 2007). This brings the disease closer to category c): *changes in microbes or in the ability to recognise emerging pathogens due to advances in the techniques of epidemiology.* The movement of the pathogen, which essentially acts like a parasite in relying on devils to propagate it spatially, has been documented (Hawkins et al 2006; McCallum et al. 2007) and suggests that the disease also belongs in category b): *movement of pathogens or vectors, via human or natural agency.*

Morse (1995) claims that in both new and spreading emerging diseases, specific contributing factors are responsible in almost all, if not all, cases; and further, that they can almost always be identified. This makes DFTD unusual in that no particular stressors have yet been identified that would help explain the emergence of the disease at the current time. The disease is also unusual in that it fulfils both of Morse's categories of emergence: the disease appeared in the population for the first time in recorded history, and then proceeded to spread rapidly in geographic range and prevalence. It has spread so rapidly, in fact, that based on evidence gathered by DPIPWE's spotlighting program (Hocking and Driessen 1992; Driessen and Hocking 1992; Southwell and Fletcher, 1993), since the first confirmed case in 1997 (Hawkins et al. 2006), the disease had by 2010 killed an estimated 84% of the total Tasmanian devil population (DPIPWE, unpublished data).

Many diseases are aided in their emergence and spread by the existence of a reservoir host. For example, bats carry a number of different viruses that may be important in generating emerging diseases in humans via intermediate hosts (Wong et al. 2007). However, DFTD as an allograft is not capable of jumping to another species. Tasmanian devils appear to be sufficiently genetically similar to each other, specifically in Major Histocompatibility Complex genes, that the cancer is able to fool the immune systems of different individuals within the same species (Siddle et al. 2007; Belov 2011). However, even their closest living relative, the spotted-tailed quoll *Dasyurus maculatus*, is sufficiently genetically distinct from the devil that its immune systems would quickly deal with an implanted tumour from a Tasmanian devil.

Rather than coming from a reservoir host, it appears that the extinction risk comes from a deviation of the disease's mode of transmission from the traditional density dependent scenario (McCallum et al. 2009), in combination with potential Allee-related and other effects on a disease-suppressed population. Bite injuries are particularly prevalent in the mating season (Hamede, McCallum and Jones 2008), suggesting that DFTD has some attributes of a sexually transmitted disease. This would mean that DFTD transmission may be at least partially frequency dependent, and therefore that it is possible that no threshold host density for disease persistence exists. If this is the case, then the disease is capable of driving its host to extinction. This conclusion is also supported by trapping and spotlighting data on local population trends. In areas where DFTD first emerged, the population has declined by an estimated 97% (DPIPWE, unpublished data).

Conservation strategy

Four overarching strategies have been suggested to manage the disease (McCallum 2008): ***isolation*** of uninfected animals, ***disease suppression*** by culling infected animals, ***selection*** for disease resistance, and ***vaccination***. Concurrent efforts are continuing on these fronts, with the current exception of disease suppression. This has been due to the failure of disease suppression to control disease during a trial in the isolated Forestier Peninsula (Lachish et al. 2010), and also based on the model prediction described in Chapter 3 that even at high levels of effort, disease suppression would likely fail (Beeton and McCallum 2011).

The continuous assessment and resultant termination of the disease suppression program is an example of effective adaptive management. Adaptive management, in general terms, has been defined as a model of natural resource management in which quantifiable goals and strategies for achieving those goals are formulated, and continuously reformulated as additional information is received (Haney and Power 1996). The idea of adaptive management in the face of complex ecological problems has become very popular, in the last decade in particular (McFadden, Hiller and Tyre 2011). However, criticism has been levelled at the effectiveness of the approach in many cases, in particular where an overly simplified view of the issues has been presented (e.g. McLain and Lee 1996) or when its use has been constrained by a lack of institutional flexibility (e.g. Allan and Curtis 2005).

In the case of the Tasmanian devil, there is a sense of desperate urgency. There are a number of different possible outcomes (Jones et al. 2007) encompassing the spectrum between total extinction and once more having disease-free devils throughout their natural range. Being able to make efficient use of available resources and time could help change which of these scenarios we see unfold. Performing efficient and flexible management now not only means ensuring that the devil survives in the shorter term, but also means buying more time until future management possibilities can be brought into effect to improve the situation further.

In the face of such pressure, gathering information about the likelihood of success of potential management actions is vital to ensure that the most efficient use of resources is being made. Detailed observation of the management process, in both its successes and failures, will not only mean better outcomes for the devil but also help inform

management of other threatened species. Disease suppression is a particularly relevant case in point. Selective culling has had mixed success in other species (Donnelly et al. 2003; Wolfe, Miller and Williams 2004; Wasserberg 2009; Hallam and McCracken 2011) and is potentially ethically controversial in many cases.

Thesis aims and outline

The aim of my thesis was to contribute to adaptive management to help the Tasmanian devil by using mathematical modelling to infer relevant information, specifically in topics where acquiring such knowledge via experiment or observation alone would be impractical. I addressed this by concentrating on two distinct but connected areas of research:

- developing, testing, and applying biologically reasonable dynamical population and disease models on a closed, spatially homogeneous population

and

- using statistical models to estimate the natural distribution and abundance of wild Tasmanian devils, and using this information to develop and test a spatial dynamical model of the interaction between the devil and its disease.

The first of these is presented in Chapters 2 to 4. In Chapter 2, I introduce a compartmental Ordinary Differential Equation (ODE) model aimed at modelling the interaction between Tasmanian devils and DFTD, and perform a dynamical systems analysis to assess its validity. I obtain results regarding the behaviour of the system under various different scenarios, some of which are described in detail. Though a generalised model, of which this model is a special case, has been analysed in

previous work (Roberts and Jowett 1996), this chapter looks at the particular model in more detail, analysing it in terms of the Tasmanian devil and DFTD.

I then extend on this model framework in Chapter 3, applying it to the problem of modelling the effects of disease suppression by selective culling on a wild population of Tasmanian devils. This work analyses the potential effectiveness of the disease suppression trial on the Forestier Peninsula in Tasmania's south east, testing different strategies in addition to that used in the trial. The chapter provides specific guidance on how to maximise the effectiveness of selective culling in the case of the Tasmanian devil, estimates the necessary effort required to successfully suppress disease. More generally, it provides an example of using modelling to assess selective culling as a management tool – as mentioned, this is currently topical, with selective culling currently a topic of debate – and demonstrates that modelling can, and should, be used to help assess its usefulness on a case by case basis.

In Chapter 4, I return to the coupled ODE model introduced in Chapter 2; this time, the model is used in combination with collected longitudinal trapping data from three sites, measuring population size and disease prevalence of populations as they change over time. Using Bayesian Markov Chain Monte Carlo (MCMC) analysis combined with trajectory matching, as described in Cooch et al. (2010), the model was fitted to these data in order to estimate model parameters such as disease latent period. Sensitivity analyses are widely used in dynamical models of ecological processes (Cariboni et al. 2007) but techniques to estimate parameters directly from complex dynamical systems are more recent (e.g. Toni et al. 2009). The method we describe

combines two simple and well-known modelling techniques, and demonstrates that parameter estimation can be quickly performed using available observational data.

The second section of the thesis explores the spatial aspect of the devil-DFTD dynamic, building on the results gained in the first. In Chapter 5, I introduce a novel approach to build an abundance map based on both trapping and spotlighting data pre-disease, using climate, topography and vegetation variables as predictors. This represents the first attempt to directly model abundance of the Tasmanian devil based on climate and vegetation data. The approach incorporates modern predictive techniques (see Elith et al. 2006) while dealing with multiple types of data and, as far as possible, incorporating model and observation error into its estimates. Though these modelling developments are individually well established, less work has been done on synthesising them in this way. This kind of analysis may be further applicable for other species where data exist in multiple forms or are relatively sparse.

Using the results from Chapter 5 as a basis, I develop a reaction-diffusion modelling framework in combination with the coupled ODE modelling framework to model the spatial spread of disease in devil populations in Chapter 6. Trajectory matching is then used to examine their fit to both trapping and spotlighting data, and the models with the best fitting parameters were determined. Deterministic models of spatial disease spread appear to have been seldom used for predictive modelling. This chapter explores the potential of the technique for further use with the devil and DFTD. The methods used should be more generally applicable to other cases where species are affected by the spread of disease on a large spatial scale.

The General Discussion in Chapter 7 summarises the key outcomes of the five research chapters. It describes the knowledge gained from this thesis in terms of the direct problem of DFTD, the realised and potential impacts on management actions to help the Tasmanian devil. I also discuss the wider implications of the thesis in providing new methodologies and perspectives to modelling populations and disease, more generally adding to the body of evidence in conservation management issues, and adding to scientific debate – in particular, regarding the circumstances under which selective culling may be effective as a management tool. Finally, I mention some relevant potential future work that would build on results gained in this thesis, and the potential benefits and implications that this work might have on conservation efforts – both for the Tasmanian devil and for other threatened species.

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Chapter 2. Dynamical Systems analysis of a model describing Tasmanian Devil Facial Tumour Disease

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Chapter 3: Models predict that culling is not a feasible strategy to prevent extinction of Tasmanian devils from facial tumour disease

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"I simply wish that, in a matter which so closely concerns the wellbeing of the human race, no decision shall be made without all the knowledge which a little analysis and calculation can provide."

- *Daniel Bernoulli,* 1760

Abstract

Culling, either of all animals or infected animals only, is often suggested as way of managing infectious diseases in wildlife populations. However, replicated experiments to investigate culling strategies are often impractical because of costs and ethical issues. Modelling therefore has an important role. Here, we describe suite of models to investigate the culling of infected animals to control an infectious cancer in the Tasmanian devil *Sarcophilus harrisii*.

The Tasmanian devil is threatened by an infectious cancer, Tasmanian devil facial tumour disease. We developed deterministic susceptible, exposed and infectious (SEI) models with differing ways of incorporating the time delays inherent in the system. We used these to investigate the effectiveness for disease suppression of various strategies for the removal of infected animals.

The predictions of our models were consistent with empirical time series on host population dynamics and disease prevalence. This implies that they are capturing the essential dynamics of the system to plausible extent.

A previous empirical study has shown that removals every 3 months did not appear to be sufficient to suppress disease in semi-isolated infected population. Our models are in accordance with this observed result. The models further predict that while more frequent removals are more likely to be effective, the removal rate necessary to successfully eliminate disease may be too high to be achievable.

Synthesis and applications: Our results, in association with previous experimental study, show that culling is unlikely to be feasible strategy for managing Tasmanian devil facial tumour disease. Similar conclusions have been reached in studies of other wildlife diseases. We conclude that a test and cull approach is rarely appropriate for controlling wildlife diseases and should only be attempted if models predict that it will be effective.

Introduction

Infectious disease threatens many wildlife populations (Smith, Acevedo-Whitehouse & Pedersen 2009; Thompson, Lymbery & Smith 2010), but managing disease in free ranging populations is difficult (Wobeser 2002). Culling, whether of all individuals regardless of infection status or targeted at infected animals only, is often suggested as a management strategy (Woodroffe et al. 2006; Davidson et al. 2009; Wasserberg et al. 2009). Culling programmes are extremely resource intensive and may be ethically controversial. It is logistically impossible to investigate many possible alternative removal strategies experimentally. Models can identify those alternatives which have the best prospects for success. Here, we describe the development of a suite of models to investigate the use of culling of infected animals to control an epidemic of an infectious cancer in Tasmanian devils *Sarcophilus harrisii* (Boitard, 1841).

Tasmanian Devil Facial Tumour Disease (hereafter DFTD) is threatening to cause the extinction of the largest surviving marsupial carnivore. Signs typical of the disease were first detected in north-east Tasmania in 1996. DFTD has subsequently spread over the majority of the range of the Tasmanian devil, leading to an overall population decline of at least 60%. Where the disease has been present for five or more years, there have been population declines in excess of 90% (Lachish, Jones & McCallum 2007) with an almost complete disappearance of individuals older than three years of age (Jones et al. 2008). DFTD is an infectious cancer in which the tumour cells themselves are the infective agent, thought to be spread between individuals by biting (Pearse & Swift 2006; Siddle et al. 2007). Much biting occurs during sexual interactions (Hamede et al. 2008). The disease may therefore have the characteristics of a sexual transmitted disease, including frequency dependent transmission

(McCallum, Barlow & Hone 2001). High prevalence of infection is maintained and ongoing population declines continue in areas where the disease is well established, consistent with transmission being frequency rather than density dependent (McCallum et al. 2009). This host-specific disease may therefore lead to the extinction of its host (de Castro & Bolker 2005) and developing strategies to prevent this outcome is critical.

There are four main management strategies that could be applied to manage DFTD: removing uninfected wild animals from exposure to infection; disease suppression through removal of infected animals; identification and dissemination of resistant genotypes; and development of a vaccine (McCallum & Jones 2006). The first approach is being applied, with over 150 wild-caught animals from currently non-diseased areas having been transferred to mainland Australian zoos. However, in the medium term (until the possible extinction of both the devil and DFTD in the wild) this strategy will not maintain wild populations in currently diseased areas. Research is currently in progress to determine whether resistant animals can be identified (e.g. Siddle et al. 2010; Woods et al. 2007) and to attempt to develop a vaccine (Woods et al. 2007), but as yet there is no clear indication that either strategy will be successful.

Disease suppression through removal of infected individuals is the only strategy that can currently be tested in the field to manage the disease in wild, infected populations. "Test and cull" is widely used to control disease in livestock, but has rarely been applied in wild animals (Wobeser 2002; but see Wasserberg et al. 2009, Treanor et al. 2011, in press). Tasmanian devils are highly trappable, DFTD is visible on external

examination and it is likely that most transmission occurs from large, friable tumours. Removal of infected individuals therefore might be expected to be effective.

The strategy has been trialled on the Forestier Peninsula, an almost completely isolated peninsula in south-east Tasmania (Jones et al. 2007; Lachish et al. 2010). The peninsula (42° 03' 53" S, 148° 17' 14" E), approximately 100 km² in area, is connected to the remainder of Tasmania by a narrow isthmus cut by a canal, across which there is a single bridge. Shortly after the arrival of the disease in mid-2004, the population size was estimated at approximately 120 individuals (Lachish et al. 2010). From June 2004 to December 2010, all individuals captured with detectable disease were removed and euthanased. Trapping within a 70 km² area of the peninsula, using 10-night trapping sessions with 40-50 traps, was conducted biannually in 2004 and 2005, increasing to four to five trapping sessions per year in 2006 onwards. The trial cost in excess of $200,000 Australian dollars per year, despite being on a relatively small spatial scale.

Mark recapture analysis estimated the probability of capture within a session at between 0.57 and 0.94, depending on the trapping session. Despite this intensive effort and these high recapture rates, there is no clear evidence to date that the removals have reduced the rate of transition from healthy to diseased status in comparison with a comparable unmanipulated site at the Freycinet Peninsula (Lachish et al. 2010).

In this paper we model the effects of removal of infected individuals on the interaction between Tasmanian devils and DFTD. Our first objective was to estimate

the likelihood of success in the long term of the removal programme on the Forestier peninsula. Our second objective was to determine whether there are modifications that could be made to this programme to increase this likelihood of success.

Materials and methods

Biology and epidemiology relevant to model structure

Tasmanian devils are seasonal breeders, with most matings occurring from mid-February to mid-March. After a short gestation (14-22 days), up to four young may be suckled, which emerge from the pouch in July through August and become independent of their mother by early February (Hesterman, Jones & Schwarzenberger 2008). Devils have a relatively short lifespan in the wild (less than six years) and can reliably be aged in the field up to the age of three (Jones, Barmuta, Sinn & Beeton, unpublished data). Few females reproduce before two years of age, although there is evidence of a substantial minority of one-year-old females carrying young in infected populations (Jones et al. 2008).

There is no clear evidence of seasonality in prevalence (McCallum et al. 2009). Tumours have been reported from very few individuals less than one year of age and prevalence is substantially lower in 1-2 year olds than in individuals older than two (McCallum et al. 2009). The disease appears to be invariably fatal, with very few individuals surviving more than six months beyond the first appearance of clinical signs. There is no evidence thus far of acquired or innate resistance to infection. The latent period of the disease is currently unknown, although there is some evidence that it may be lengthy - up to 12 months (Pyecroft et al. 2007).

Model structure

We used an SEI (Susceptible-Exposed- Infectious) framework, with no resistant class. In all but our initial model, we explicitly included age structure. Age structure and associated time delays are critically important in this system. Both mortality and fecundity are strongly age dependent, as is disease transmission (see McCallum et al. 2009). In addition, the latent period of the disease needs to be dealt with as a distributed delay. We investigated a range of ways of incorporating time delays because the way in which they are modelled can have both qualitative and quantitative effects on model predictions.

There are many ways to incorporate age structure and time delays such as the latent period into epidemiological models. Matrix-based models (Caswell 1989) are useful for dealing with discrete age classes; however, stability problems as a result of nonlinearity can arise when the iteration timestep used in these models is too large, (Gyllenberg, Hanski & Linstrom 1997; Henson 1998). They are often appropriate when epidemic processes are completed within a single timestep (Gerber et al. 2005), which is not the case for DFTD (McCallum et al. 2009). We therefore used models that are continuous in time, which are often more useful for dealing with time dependencies that occur on multiple scales, such as the seasonal breeding in the Tasmanian devils and the latent period in the tumour.

All models were implemented using the R programming language (version 2.10.1, R Development Core Team 2009).

Simple SEI model

We began with a very simple and widely used (e.g. Anderson & May 1991) Ordinary Differential Equation (ODE) model, in which the population is separated into three classes: Susceptible (S), Exposed (E) and Infectious (I). Following empirical evidence from McCallum et al. (2009), we assumed frequency-dependent transmission. The model also included logistic density dependence in host fecundity in the absence of disease. We modelled removals proportional to the size of the infected population I at a constant per capita rate per unit time ρ (see Appendix 3.1S in Supporting Information for more information).

The coupled ODE system takes this form:

$$dS/dt = bN(1 - N) - \mu S - f(S; I; N) \quad (1)$$

$$dE/dt = f(S; I; N) - (k + \mu)E \quad (2)$$

$$dI/dt = kE - (\mu + \alpha + \rho)I \quad (3)$$

The total population is represented by N, where $N = S + E + I$. Here t represents time in years, b is the birth rate per animal per year, μ is the mortality rate in the absence of disease, $k = 1/L$ models the latent period L of the disease, α is the disease-specific mortality rate, ρ represents the removal effort on infectious animals, and $f(S; I; N) = \beta SI/N$ is the frequency-dependent transmission function. The populations have been scaled by carrying capacity to make S, E, I and N dimensionless.

The model has three equilibrium scenarios which can be calculated analytically: host extinction ($S = E = I = 0$), disease eradication, ($S = N$, $E = 0$, $I = 0$) and disease-host coexistence. When varying the removal rate ρ, there are two bifurcation points that define the points of transition between equilibria. The first (ρ_1) represents the point at

which the removal effort is enough to avoid host extinction but not eliminate disease, whereas the second (ρ_2) represents a removal rate sufficient to eradicate disease from the host population.

Age structured ODE model

To introduce age structure, we separated population classes *S*, *E* and *I* into age classes S_i, E_i and I_i with i = 0 to 4, representing age classes 0-1, 1-2, 2-3, 3-4 and 4+ respectively.

In our simple SEI model, the time delay associated with the latent period has a negative exponential distribution, which is unlikely to be a plausible representation of the actual distribution of latent periods. A more realistic and flexible way of modelling distributed delays (Wearing, Rohani & Keeling 2005) is to create *m*-1 intermediate classes between stages, each with exponential transfer. The probability distribution of transfer from one stage to the next then becomes a gamma distribution $\Gamma(m,1/m)$. As m increases, the mean remains constant at one but the variance decreases, with large *m* approximating a delta function $\delta(t\text{-}1)$, as is assumed by a matrix model approach. We applied this approach to both the age structure (with *m*-1 classes) and latent period (with *n*-1 classes).

As all reproduction does not occur on a single date, a distributed delay is actually a more realistic assumption than a fixed delay. We chose a value of m = 10, which corresponds to a variance in the one-year age class transition of 0.1 years. It is highly likely that the latent period is variable with a frequency distribution depending on the infective dose, the genotype of the recipient and the site of infection. The limited empirical information available (Pyecroft et al. 2007) includes anecdotal observations

of latent periods between 3 and 12 months; $n = 4$ approximates this amount of variability. The system of equations for this model can be found in Appendix 3.2S in Supporting Information.

We used three different pairings of m and n in our results.

1. $m = 1$ and $n = 1$, a basic coupled ODE model with no intermediate steps between age classes or Exposed classes.
2. $m = 10$ and $n = 4$, using a narrow distribution for ageing and making a best guess at the latent period distribution.
3. $m = 10$ and $n = 10$, using a narrow distribution for both the ageing and latent period distributions.

Delay Differential Equation model

An alternative way of handling time delays is to use Delay Differential Equations (DDEs) (Taylor & Carr 2009), which incorporate an explicit delay in both ageing and transfer between the Exposed and Infectious classes. These models are much more efficient than the coupled ODE model in terms of memory and computation time. A necessary simplifying assumption that ageing does not occur in the Exposed and Infectious classes was made. This should not make a large difference to the model results: with our parameter estimates, the time period from infection to death will be nine months on average, so devils will age at most a year in the model structure. The system of equations for this model is contained in Appendix 3.3S in Supporting Information.

Bifurcation diagrams

Exact solutions for the fixed points of the age-structured equations were not possible: we therefore obtained bifurcation diagrams numerically to show the behaviour of equilibrium states with respect to changing removal effort. We modelled naive devil populations beginning at carrying capacity and with a stable age distribution, then introduced a small number of diseased animals (we arbitrarily used 1% of the population) and iterated the model over 200 years; a period sufficient for steady state to be reached.

Parameter estimates

We derived estimates of devil demographic parameters (shown in Table 3.1S in Supporting Information) from current knowledge of devil life history. Appropriate estimates for the parameters associated with disease transmission, particularly the latent period L and the initial rate of increase in prevalence following disease introduction r_0, are harder to obtain (see below). We also used extensive sensitivity analysis to investigate the effect of these parameters on our model predictions.

We estimated β_c, the effective contact rate between age classes for which transmission exists, from the value of $\lim_{P\to 0}\frac{1}{P}\frac{dP}{dt}=r_0$ calculated from the model that matched a given estimate of r_0, where P is the prevalence in adult devils (over 1 year of age). The parameter r_0 here represents the initial rate of increase in prevalence of DFTD after initial introduction.

Estimates of r_0 are available from two populations for which good prevalence data exist from the time of first disease appearance: the Freycinet Peninsula (42° 03’ 53”

S, 148° 17' 14" E), r_0 = 1.0055 and Fentonbury (42° 38' 55" S, 146° 46' 01" E), r_0 =2.2644 (McCallum et al. 2009). Unless otherwise stated, we used the value of r_0 from Fentonbury in preference to the value from Freycinet, as at Freycinet the localised rate of increase of disease has probably been confounded with spatial spread of the disease. The study site is a peninsula about 5 km wide and extending some 50 km from north to south, which was progressively overtaken by disease over five years. In contrast, the Fentonbury site is more compact, being approximately 5 x 5 km, and the measured rate of increase of prevalence is likely to be a better indication of local increase.

For most of the first year of their lives, devils live in the den (Guiler 1970). As there is no evidence of vertical transmission of the disease and infection in animals less than one year of age is extremely rare (McCallum et al. 2009) we assumed that devils in the 0-1 age class are not a significant part of the infection process - hence in our models $\beta_{i,j}$ is defined as 0 for $i = 0$ or $j = 0$ where $\beta_{i,j}$ represents transmission from an animal of age i to one of age j. There is also evidence that the rate of transmission in 1-2 year olds is lower than for older animals – for example, at Fentonbury the transmission rate amongst 1-2 year olds is 0.602 times that of older animals (McCallum et al. 2009). Thus we set $\beta_{i,j}$ as $0.602\beta_c$ for $i = 1$ or $j = 1$, where i and j are both positive. For other age classes, it is set to β_c. There is no evidence of any consistent sex bias in prevalence (McCallum et al. 2009), so sexes are treated as identical in this model.

Suppression methods

We investigated four potential disease suppression strategies:

1. Removing a proportion of infected devils continuously, as in the simple ODE model. This is the simplest strategy to model, but continual trapping is difficult in practice.
2. Removing a proportion of infected devils discretely every three months. This was the approach implemented in the Forestier Peninsula trial.
3. Removing a proportion of infected devils discretely every month. An increase in the frequency of trapping trips is a potential modification to the existing strategy.
4. Removing a proportion of infected devils continuously, while adding the same number of healthy devils. This last strategy is unlikely to be feasible but is included to separate the effects of removal of diseased devils from the effect of reducing population size by culling.

Fit to observed time-series data

We used population and disease data (Lachish, Jones & McCallum 2007; Lachish et al. 2010) to assess our model predictions in comparison to real data. First, we fitted the model to data from the control population on the Freycinet peninsula site, where no removals were undertaken. The goodness of fit function was defined as the sum of squares of the difference of the model data from the population data at each point in time where the population data was collected, weighted inversely by the appropriate confidence interval for the population data. The model was fitted using two parameters: the carrying capacity (as the model is dimensionless) and the initial value of disease prevalence at the time when the disease was first found in the population. All other parameters were as defined above. Note that the devil demographic parameters and r_0 were obtained from this same population over the same time period, although in a separate analysis (McCallum et al 2009). In each run of the model, the

simulated population represented a healthy stable-age distribution until the time of disease outbreak, at which point a proportion of the population equal to the set disease prevalence was transferred to the infected class.

We then fitted the model to data from the removal trial at the Forestier Peninsula (Lachish et al. 2010). In this case, we fitted four parameters; the two used above, with the additional parameters of continuous removal effort and r_0, which is likely to differ between Forestier and Freycinet. In addition, we calculated the goodness of fit function for the model's prevalence output in an identical fashion to the above population estimate fitting. The overall goodness of fit function for the model is the sum of the two functions – the model is thus fitted to both the population and prevalence data with approximately equal weighting (the population size is scaled to between 0 and 1, as is prevalence). In this case, the model began with the initial conditions of a diseased population with prevalence set by the fitting parameter. At the time known to be the beginning of disease suppression, the value of ρ in our model is changed from zero to our fitting parameter value. This ad hoc model fitting procedure was intended to determine whether our model was qualitatively in agreement with the observed pattern, in contrast with more formal approaches such as approximate Bayesian computation (Toni et al. 2009) or trajectory matching (Cooch et al. 2010), which would require more data than we had available.

Results

Bifurcation diagrams

Figure 3.1 shows a bifurcation diagram of the stability behaviour of equilibrium states of the basic SEI model with respect to the removal rate ρ. If the population becomes disease-free at equilibrium then increasing the removal rate further than necessary can

cause a transition into extinction, but this situation does not occur here for any biologically realistic parameter estimates.

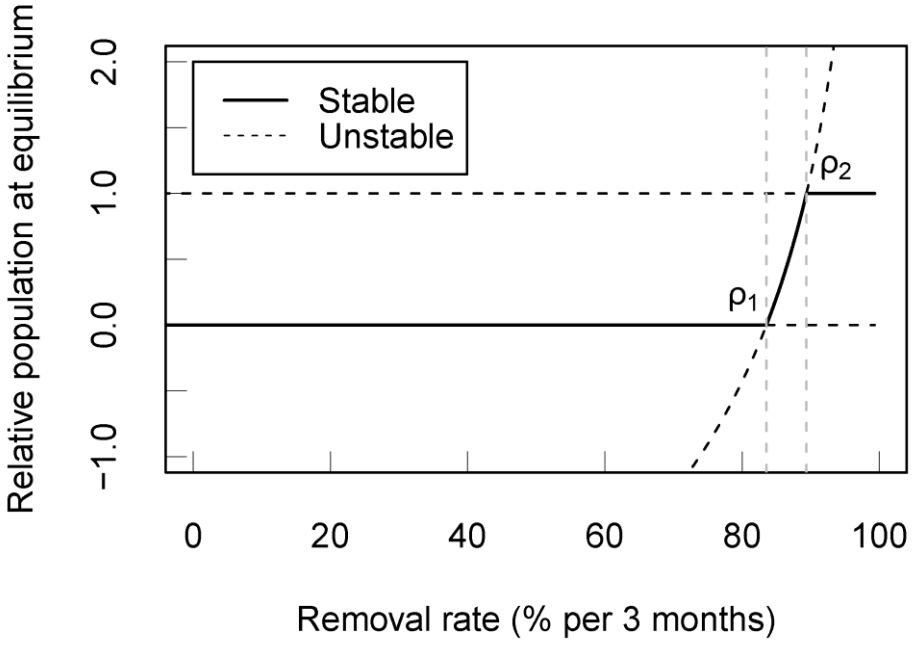

Figure 3.1
Bifurcation diagram for basic SEI model. The two vertical dotted lines represent the transition points ρ_1 *and* ρ_2*. Parameter values from Table 3.1S.*

Figure 3.2 shows a bifurcation diagram obtained numerically from the age structured ODE model with gamma distributed delays. The prevalence is the proportion of infected adults in the stable state after 200 years (we did not observe any periodic or quasi-periodic outcomes for our parameter values). The Time To Extinction (TTE) is the amount of time required for the population to reach 1% of the carrying capacity, provided this event occurs within 200 years. In all our numerical results, ρ_1 and ρ_2 represent the points at which 1% and 99% of the population persist respectively, instead of 0% and 100% as in the analytical case.

Without removals, all model variants predicted extinction of the devil population within 10 years. With continuous removal, there was no marked increase in the expected time until extinction until removal rates were close to ρ_1 (Fig. 3.2). However, Figure 3.2 further shows that between the two transition points, prevalence is low (<3%), declining to zero at ρ_2. Devil populations can thus only coexist with the disease in the long term for low levels of prevalence. As most of the dynamical information can be summarised by giving the parameters ρ_1 and ρ_2, Table 3.1 provides a comparison of these parameters for the different removal strategies.

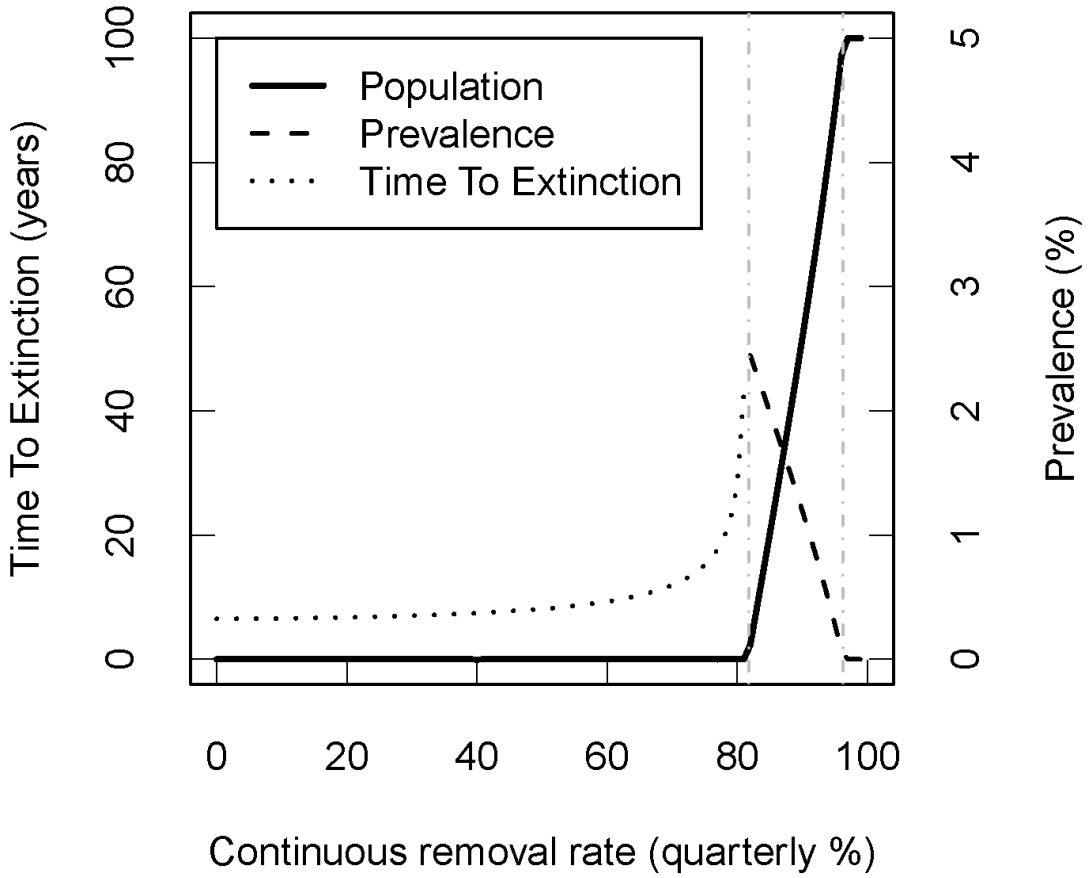

Figure 3.2
Plot of relative equilibrium population, equilibrium disease prevalence and time to extinction against removal rate for the coupled ODE method with m *= 10,* n *= 4 and for Strategy 1. Parameter values from Table 3.1S. State changes occur at* ρ_1 *= 80.67% and* ρ_2 *= 95.86% as indicated by the grey dotted vertical lines.*

Table 3.1

Transition point values for varying modelling methods and strategies. ρ_1 represents the minimum removal rate which avoids host extinction but does not eliminate disease in the model; ρ_2 represents the minimum removal rate which eradicates disease from the host population. The table contains "-" if no removal rate will achieve the goal for the given combination of model and strategy. To enable comparisons, the transition points are expressed in terms of percentage of animals removed per quarter, even where the removal rate is continuous or monthly. Parameter values from Table 3.1S.

Strategy	Simple SEI model		Coupled ODE model				DDE model	
			m=1, *n*=1		*m*=10, *n*=4		*m*=10, *n*=10			
	ρ_1	ρ_2	ρ_1	ρ_2	ρ_1	ρ_2	ρ_1	ρ_2	ρ_1	ρ_2
1 (continuous removal)	84.18	89.85	62.82	89.21	79.03	96.21	83.77	97.47	92.08	98.02
2 (monthly removal)	84.51	90.72	61.94	90.01	78.94	97.49	84.16	98.61	-	-
3 (quarterly removal)	-	-	69.81	-	94.31	-	-	-	-	-
4 (quarterly removal of infected with replacement)	80.74	-	49.48	-	64.65	-	70.42	-	-	-

Sensitivity analysis

Of the models presented, the most representative of the actual population is probably the coupled ODE model with m = 10 and n = 4. For this model, Figure 3.3 shows contours of the removal rates necessary for disease elimination (ρ_1) and prevention of host extinction (ρ_2) as a function of the latent period and the rate of increase per year in prevalence following first disease introduction r_0.

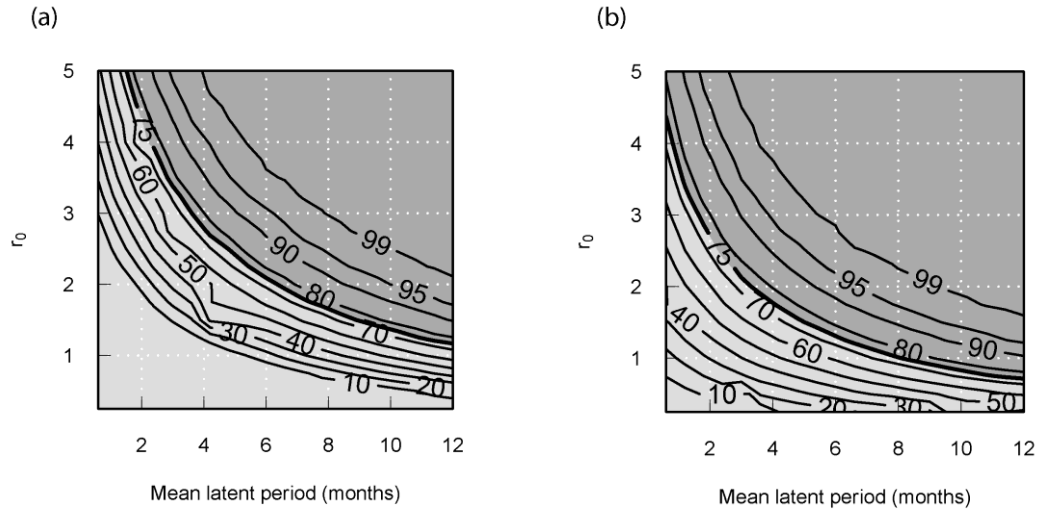

Figure 3.3
Sensitivity analysis for varying latent period L *and disease parameter* r_0 *holding all other parameters constant at the default values with* ρ_1 *(Fig. 3.3a) and* ρ_2 *(Fig. 3.3b) as the response variables. The* m=*10,* n=*4 model is used here with a continuous removal strategy. The black line at 75% is an estimate of the maximum removal effort possible, taking into account the existence of a cryptic population.*

Data fitting

For the Freycinet peninsula, we found a best fit carrying capacity value of 121 and an initial prevalence value of 1.27%, which corresponds to about two adults being initially infected. The model results (see Fig. 3.4) for the most part lie within the confidence intervals of the real population estimates, though the model fit appears to

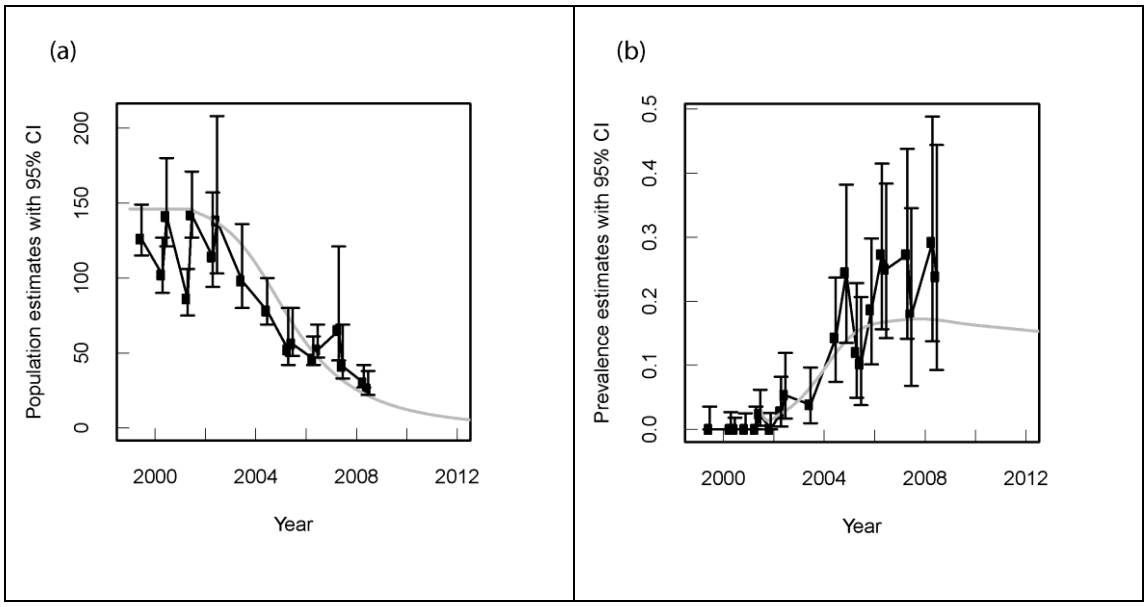

Figure 3.4
Comparison of model to Freycinet data. The black line represents the actual estimate of the population (Fig. 3.4a) and prevalence (Fig. 3.4b) in the Freycinet peninsula from trapping surveys, with 95% confidence intervals. The grey line represents the best fit model estimate of disease progression. The m*=10,* n*=4 model is used here with a continuous removal strategy.*

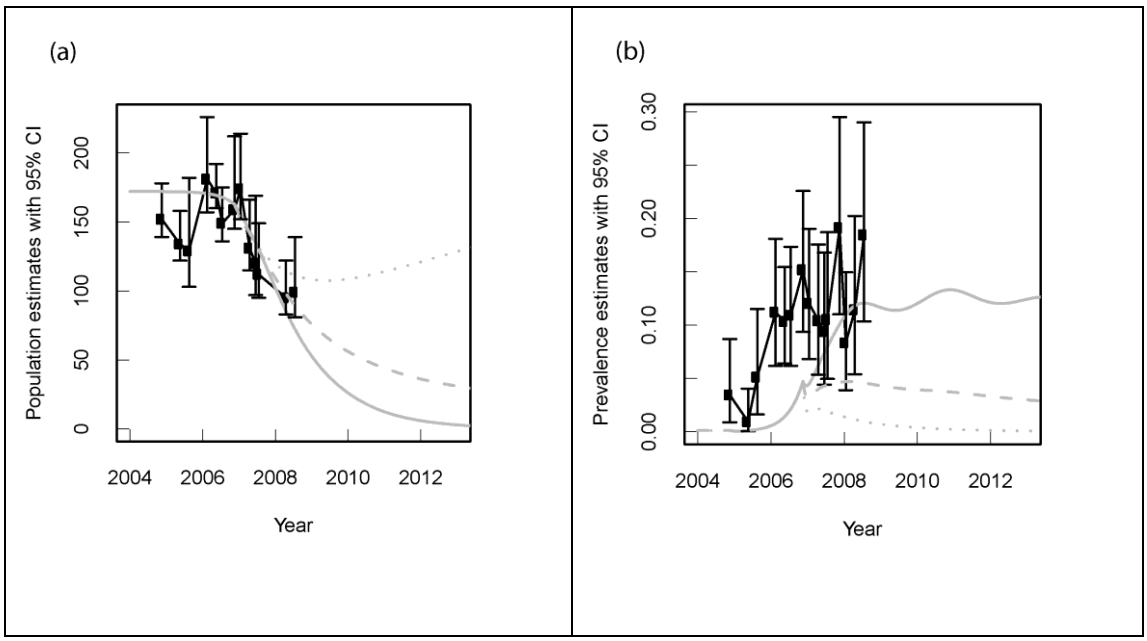

Figure 3.5
Modelling potential disease suppression scenarios. The black line represents the actual estimate of the population (Fig. 3.5a) and prevalence (Fig. 3.5b) in the Forestier peninsula from trapping surveys, with 95% confidence intervals. The solid grey line represents the best fit model, whereas the dashed line represents increasing removal effort in this model above ρ_1 *(90%) and the dotted line above* ρ_2 *(99%). The* m*=10,* n*=4 model is used here with a continuous removal strategy.*

overestimate the population in or around 2005. For the suppression trial at the Forestier Peninsula, we found a best fit carrying capacity value of 172, an initial prevalence value of 0.09%, an r_0 value of 2.5092 and a quarterly continuous removal effort of 69.0%. Though the fit is not highly sensitive to the latter parameter, this value corresponds with what we would expect from the field trapping effort. The best-fit value for r_0 is slightly higher than that found at Fentonbury (2.2644; McCallum et al. 2009) but well within the estimated 95% confidence interval.

The results (see Fig. 3.5) again appear to compare well in the case of the population estimate, with the model results only lying outside the confidence intervals of the real population estimates at one point in the time series. However, the model generally underestimated prevalence. The two additional scenarios involving an increased removal effort demonstrate the time scale in which we are likely to see results if disease suppression is successful, or is made successful. In each case, only a few years are required to tell what the likely long-term outcome is likely to be – in the 90% case, disease coexistence with its host; and in the 99% case, total disease eradication.

Discussion

Empirical analysis suggests that an attempt to manage DFTD by removal of infected individuals on the Forestier Peninsula has not, after 2.5 years, resulted in a decline in prevalence or population recovery (Lachish et al. 2010). A primary objective of this modelling exercise was to investigate whether higher removal rates or different removal strategies might have been successful. Given the results in Table 3.1, it appears that a very high removal rate would be required to remove disease or even to

prevent host extinction. The current strategy of removing individuals on three-monthly field trips is unlikely to be effective. If removal occurs on a continuous basis, prospects for managing the disease are improved, simply because the mean time for which an infected animal remains in the population before removal is reduced. However, continuous removal is difficult logistically, requiring trapping teams to be working continuously. It is also is likely to result in trap fatigue and lowered capture rates.

In excess of 20% of the devil population at the Forestier trial removal site is never caught in traps, based on recent DNA analysis of scats and hair samples (Jones, M.E. *pers comm*). The maximum possible removal rate of infected devils is thus less than 80%. Given our results, this obviously presents a pessimistic picture of the potential success of disease suppression. Finding ways to deal with trap-shy animals is vital.

The conclusion that a very high removal rate is needed is independent of the details of the model, although Table 3.1 shows that incorporation of realistic delay distribution increases the removal rate necessary.

Our results emphasise the influence of time delays and the way in which they are modelled. The results for the Coupled ODE model with $m = 10$ and $n = 10$ are substantially different to those for the DDE model. This could be due to the assumption made in the DDE model that animals do not age once they are exposed to the disease, or to the difference between the distributions of ageing and latent period between the models. A much higher value for m in the coupled ODE model would more closely approximate the DDE model, shedding light on the impact of these

structural differences. Nevertheless, the gamma distributed delay approach of Wearing, Rohani & Keeling (2005) provides a powerful means of realistically including distributed delays.

From the sensitivity analysis it is evident that the longer the latent period, the more difficult it is to eliminate disease or prevent host extinction. This is not surprising, because for a given rate of increase in prevalence r_0, the basic reproductive number R_0 increases with latent period (McCallum et al. 2009). Unfortunately, there is still little more than anecdotal information available on the frequency distribution of the latent period for DFTD. For the rates of increase in prevalence observed in the field, which are in the range 1-2.25 y^{-1}(McCallum et al. 2009), it is clear from Figure 3.3 that a removal strategy is unlikely to be successful if the mean latent period is in excess of about six months. On the other hand, if the mean latent period is three months or less the prospect of successful disease suppression is much greater.

The model fitting in Figure 3.4 suggests that the model is capable of capturing the main trends in both population size and prevalence on the Freycinet Peninsula. The prevalence is not as well modelled for the Forestier Peninsula as was the case of Freycinet: the model fails to capture the initial rapid increase in prevalence, despite the fitted value of r_0 being in excess of the value estimated for either the Freycinet or Fentonbury populations. This may be because the model is assuming a continuous removal, whereas in reality removal occurs at three-monthly intervals. However, the lack of fit may also be due to a number of unmodelled effects – for example, the transmission process may differ between sites, as transmission is unlikely to be purely frequency dependent (see Chapter 4 for a discussion of this).

Coexistence of Tasmanian devils and the tumour was possible for only a very small range of removal rates. This is a consequence of frequency dependent transmission and means that in this particular case, a stochastic model would provide limited additional information. Either the removal rate is sufficient for control of infection or it is not, and issues such as stochastic extinction of the host at low density or fadeout of the pathogen at low prevalence are unlikely to be important.

Heterogeneity in the structure of the host population and in contact rates is potentially more important. We have assumed that all devils are equally susceptible to disease. Selective removal of infected animals (which by definition would have susceptible genotypes) might have the additional benefit of increasing the probability that resistant animals would breed with each other. However, recent analysis of MHC types in Tasmanian devils shows that the majority of devils in the Forestier area have MHC types indistinguishable from the tumour and that this area has particularly low MHC diversity in comparison with devil populations in the rest of Tasmania (Siddle et al. 2010). We have also omitted the observed increased breeding by 1 to 2 year old females in populations affected by DFTD (Jones et al. 2008; Lachish, McCallum & Jones 2009). Continuing population decline in diseased populations (Lachish, Jones & McCallum 2007; Lachish, McCallum & Jones 2009) shows that this increased breeding is not sufficient to compensate for the effects of disease.

We have modelled transmission using a mean field assumption. Contact networks in Tasmanian devils are significantly different from randomly connected networks (Hamede et al. 2009) but they do not have a high degree of aggregation (which would facilitate transmission relative to a random network); nor do they have high levels of

transitivity (which would inhibit transmission relative to a random network). It is therefore unlikely that culling would produce major changes in the structure of the devil contact networks.

Conclusion

Our modelling shows that managing DFTD through selective culling is difficult, despite high trappability and the ability to diagnose infection by inspection on capture. As transmission is frequency dependent, disease progresses rapidly and is likely to lead to host extinction within 1 to 2 decades without intervention. Nevertheless, the models show that density dependent transmission is not a precondition for selective culling to be a feasible control strategy for wildlife populations: a sufficiently high removal rate of diseased animals is capable of eliminating or suppressing disease. A diagnostic test capable of detecting disease before exposed individuals become infectious would substantially reduce the removal rate necessary.

Several other studies, based on both empirical and modelling approaches, have found that culling is rarely viable as a strategy for controlling wildlife disease. Hallam & McCracken (2011) found that culling did not control white nose syndrome in bats for any of the scenarios they explored through simulation modelling. Localised culling of badger populations in the UK to control bovine tuberculosis infection appears sometimes to actually increase disease prevalence by disrupting badger social structure (Donnelly et al. 2003; Donnelly et al. 2006; Woodroffe et al. 2006). Using a spatially specific stochastic model, Davidson et al. (2009) suggested that very high culling levels and multiple culls were required to control paratuberculosis in rabbits. Wasserberg et al (2009) modelled managing chronic wasting disease in deer by selective culling, assuming both density dependent and frequency dependent

transmission. Culling was much more effective when transmission was density dependent. Theoretically, unselective culling can actually increase disease prevalence if transmission is frequency dependent (Choisy & Rohani 2006). This outcome relies on the pathogen being strongly immunising and on the presence of density-dependent regulation of the host population. Culling can then increase the proportion of susceptible individuals in the population. We recommend that culling should only be attempted once appropriate models have shown it is likely to be effective.

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Supporting Information

Appendix 3.1S: Analysis of the ODE system.

The coupled ODE system:

$$\begin{aligned}\frac{dS}{dt} &= bN(1-N) - \mu S - \frac{\beta SI}{N} \\ \frac{dE}{dt} &= \frac{\beta SI}{N} - (k+\mu)E \\ \frac{dI}{dt} &= kE - (\mu+\alpha+\rho)I\end{aligned}$$

These yield equilibrium equations:

$$\begin{aligned}bN(1-N) &= \mu S + \frac{\beta SI}{N} \\ \frac{\beta SI}{N} &= (k+\mu)E \\ E &= \frac{\mu+\alpha+\rho}{k}I \\ N &= S+E+I\end{aligned} \qquad (1\text{-}4)$$

Substituting (3) into (2) gives (where $I \neq 0$):

$$S = \frac{x}{\beta}N \qquad (5)$$

where

$$x = \frac{(k+\mu)(\mu+\alpha+\rho)}{k}$$

And substituting (5) into (1):

$$bN(1-N) = x\left(\frac{\mu}{\beta}N + I\right) \qquad (6)$$

Substituting (3) into (4) gives:

$$N = S + \left(1 + \frac{\mu+\alpha+\rho}{k}\right)I$$

so

$$I = \frac{k(N-S)}{k+\mu+\alpha+\rho}$$

and thus, using (5),

$$I = y\left(1-\frac{x}{\beta}\right)N \tag{7}$$

where

$$y = \frac{k}{k+\mu+\alpha+\rho}$$

So substituting (7) into (6):

$$\begin{aligned} bN(1-N) &= x\left(\frac{\mu}{\beta}N + y\left(1-\frac{x}{\beta}\right)N\right) \\ &= \left[x\frac{\mu}{\beta} + xy(1-\frac{x}{\beta})\right]N \\ &= \left[xy + \frac{x}{\beta}(\mu - xy)\right]N \end{aligned}$$

and so we have the quadratic

$$0 = bN^2 + \left[xy + \frac{x}{\beta}(\mu - xy) - b\right]N$$

with two solutions. The trivial solution

$$N = 0$$

implies that $S = E = I = 0$ from (5), (7) and (3), and thus represents an extinction state.

The other solution is:

$$\begin{aligned} N &= \frac{1}{b}\left(b - \left[xy + \frac{x}{\beta}(\mu - xy)\right]\right) \\ &= 1 - \frac{x}{b\beta}\left(\beta y + \mu - xy\right) \\ &= 1 - \left(\frac{(k+\mu)(\mu+\alpha+\rho)}{b\beta k}\right)\left(\frac{\beta k - k(\alpha+\rho)}{k+\mu+\alpha+\rho}\right) \end{aligned}$$

so

$$N = 1 - \frac{(k+\mu)(\mu+\alpha+\rho)(\beta-\alpha-\rho)}{b\beta(k+\mu+\alpha+\rho)} \tag{8}$$

which represents a steady state with a stable population with disease present (nonzero populations in *S*, *E* and *I*).

The third solution - where $I = 0$ as excluded in (5) and thus $E = 0$ (but $N = S \neq 0$) - is easily solvable from (1):

$$bN(1-N) = \mu N$$

so

$$N = S = 1 - \frac{\mu}{b}$$

and this represents a disease-free equilibrium state.

The Jacobian of the ODE system is

$$J = \begin{bmatrix} b(1-2N) - \mu - \frac{\beta I(N-S)}{N^2} & b(1-2N) + \frac{\beta SI}{N^2} & b(1-2N) - \frac{\beta S(N-I)}{N^2} \\ \frac{\beta I(N-S)}{N^2} & -\frac{\beta SI}{N^2} - (k+\mu) & \frac{\beta S(N-I)}{N^2} \\ 0 & k & -(\mu+\alpha+\rho) \end{bmatrix}$$

For the healthy equilibrium at $(S,E,I) = (1 - \frac{\mu}{b}, 0, 0)$, this simplifies to:

$$J = \begin{bmatrix} \mu - b & 2\mu - b & 2\mu - b - \beta \\ 0 & -(k+\mu) & \beta \\ 0 & k & -(\mu + \alpha + \rho) \end{bmatrix}$$

with characteristic equation:

$$|J - \lambda I| = (\mu - b - \lambda)[(k + \mu + \lambda)(\mu + \alpha + \rho + \lambda) - \beta k]$$

Thus

$$\begin{aligned} \lambda_1 &= \mu - b \\ \lambda_{2,3} &= \frac{1}{2}\left(-(2\mu + \alpha + k + \rho) \pm \sqrt{(2\mu + \alpha + k + \rho)^2 - 4[(k+\mu)(\mu + \alpha + \rho) - \beta k]}\right) \end{aligned}$$

So for a stable equilibrium, require

$$4[(k + \mu)(\mu + \alpha + \rho) - \beta k] > 0$$

$$\beta < \frac{(k + \mu)(\mu + \alpha + \rho)}{k}$$

and $b > \mu$. Otherwise the equilibrium will be a saddle point.

And for real values of $\lambda_{2,3}$, require

$$4[(k + \mu)(\mu + \alpha + \rho) - \beta k] < (2\mu + \alpha + k + \rho)^2$$

$$\beta < \frac{4(k + \mu)(\mu + \alpha + \rho) - (2\mu + \alpha + k + \rho)^2}{4k}$$

otherwise the equilibrium will be a stable node (assuming $b > \mu$).

The requirement for stability of the healthy equilibrium can be rearranged in terms of ρ:

$$\rho > \frac{\beta k}{k+\mu} - \mu - \alpha$$

Thus

$$\rho_2 = \frac{\beta k}{k+\mu} - \mu - \alpha$$

is the required removal rate above which a healthy equilibrium is stable, and below which a diseased population occurs.

To calculate ρ_1, we observe the value at which N in (8) reaches zero, meaning that the stable diseased equilibrium exchanges stability with the extinction equilibrium.

So $N = 0$ implies

$$\frac{(k+\mu)(\mu+\alpha+\rho)(\beta-\alpha-\rho)}{b\beta(k+\mu+\alpha+\rho)} = 1$$

and

$$(k+\mu)(\mu+\alpha+\rho)(\beta-\alpha-\rho) = b\beta(k+\mu+\alpha+\rho)$$

This can be expressed as a quadratic in $\rho + \alpha$:

$$(\rho+\alpha)^2 + \left(\mu - \beta\left(1 - \frac{b}{k+\mu}\right)\right)(\rho+\alpha) + b\beta - (\mu+b) = 0$$

Where we let

$$B = \mu - \beta\left(1 - \frac{b}{k+\mu}\right)$$

Solving gives:

$$\rho_1 = \frac{1}{2}\left(-B \pm \sqrt{B^2 - 4\beta(b-\mu)}\right) - \alpha$$

as the required removal rate above which a diseased but stable population exists, and below which extinction occurs.

We can also use the next-generation method (described in Heffernan et al., 2005) to solve for ρ_2:

$$F = \begin{bmatrix} 0 & \frac{\beta S(N-I)}{N^2} \\ 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & \beta \\ 0 & 0 \end{bmatrix}$$

$$V = \begin{bmatrix} k+\mu & 0 \\ -k & \mu+\alpha+\rho \end{bmatrix}$$

$$V^{-1} = \frac{1}{(k+\mu)(\mu+\alpha+\rho)} \begin{bmatrix} \mu+\alpha+\rho & 0 \\ k & k+\mu \end{bmatrix}$$

$$FV^{-1} = \frac{1}{(k+\mu)(\mu+\alpha+\rho)} \begin{bmatrix} 0 & \beta \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \mu+\alpha+\rho & 0 \\ k & k+\mu \end{bmatrix}$$

$$= \frac{1}{(k+\mu)(\mu+\alpha+\rho)} \begin{bmatrix} \beta k & \beta(k+\mu) \\ 0 & 0 \end{bmatrix}$$

$$\lambda = 0, \frac{\beta k}{(k+\mu)(\mu+\alpha+\rho)}$$

$$R_0 = \frac{\beta k}{(k+\mu)(\mu+\alpha+\rho)}$$

so

$$\rho_2 = \frac{\beta k}{k+\mu} - \mu - \alpha$$

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Table 3.1S: Parameter estimates used for models.

Parameter	***Estimate***	***Source and notes***
Median life expectancy	4 years	Arbitrary estimate based on maximum lifespan in wild (6 years). Because the growth rate in the model is kept at a fixed value by increasing fecundity, the results are not highly sensitive to this parameter. See Appendix 3.4S for further analyses.
Median life expectancy with disease	3 months	Few records of survival with disease more than six months from first clinical signs (McCallum et al., 2009)
Latent period of disease	Sensitivity analysis between 3 months and one year	
Maximum population increase rate	25% $year^{-1}$	In the range likely for a mammal of the size of a devil using allometric models (McCallum, 2000).
Age-dependent fecundity (*bi)*	0, 0.13, 1.3, 1.65 and 1.21 for $i = 0$ to 4	Optimisation procedure, (*optimize* in R (Brent, 1973),) used to scale the fecundity values from Lachish (2007) so that when the model is run, the maximum population increase per year in a naive population, calculated as $\lim_{N\to 0} \frac{1}{N}\frac{dN}{dt} = r$ where r is the Malthusian parameter, matched the assumed value of ln(1.25).
Annual survival probability (*si*)	0.453, 0.512, 0.538 and 0.256 for i = 1 to 4	Mark recapture estimates from Lachish et al (2007). As these include a component of permanent emigration, scaled to match the assumed median life expectancy of 4 years. Converted to mortality rates (μ_i) using the formula $\mu_i = -\ln(s_i)$.
Juvenile survival probability s_0	0.449 (unscaled)	Assumed that juveniles (0-1 year olds) survive so long as their mother survives while they are dependent - approximately the first 9.5 months of life (see Guiler, 1970) - and experience the same mortality as a 1-2 year old devil for the remaining 2.5 months. Thus $s_0 = \left(9.5\sum_i b_i s_i / \sum_i b_i + 2.5 s_1\right)/12$

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Appendix 3.2S: Description of the age-structured SEI system.

Below is a description of the age-structured SEI system as separated into subgroups as described in the main article.

Here $S_{a,i}$ and $I_{a,i}$ represent subgroup *i* (which varies from 1 to *m*) of age class *a* of the susceptible (*S*) and infectious (*I*) compartments respectively. $E_{a,i,j}$ represents subgroup *i* of age class *a* and latent period subgroup *j* (which varies from 1 to *n*) of the exposed (*E*) compartment. The dummy variable *k* is used here for summation over indices.

$$N = \sum_k N_k$$

$$\frac{dS_{0,1}}{dt} = (\sum_k b_k N_k)(1 - N) - (\mu_0 + m)S_{0,1}$$

$$\frac{dS_{a,1}}{dt} = -(\frac{1}{N}\sum_k \beta_{a,k} I_k + \mu_a + m)S_{a,1} + mS_{a-1,m}$$

$$\frac{dS_{a,i}}{dt} = -(\frac{1}{N}\sum_k \beta_{a,k} I_k + \mu_a + m)S_{a,i} + mS_{a,i-1}$$

$$\frac{dE_{a,1,1}}{dt} = \frac{1}{N}S_{a,1}\sum_k \beta_{a,k} I_k + mE_{a-1,m,1} - (m + dn + \mu)E_{a,1,1}$$

$$\frac{dE_{a,i,1}}{dt} = \frac{1}{N}S_{a,i}\sum_k \beta_{a,k} I_k + mE_{a,i-1,1} - (m + dn + \mu)E_{a,i,1}$$

$$\frac{dE_{a,1,j}}{dt} = mE_{a-1,m,j} + dnE_{a,1,j-1} - (m + dn + \mu)E_{a,i,j}$$

$$\frac{dE_{a,i,j}}{dt} = mE_{a,i-1,j} + dnE_{a,i,j-1} - (m + dn + \mu)E_{a,i,j}$$

$$\frac{dI_{a,1}}{dt} = dnE_{a,1,n} + mI_{a-1,m} - (\mu_a + \mu_I + r + m)I_{a,1}$$

$$\frac{dI_{a,i}}{dt} = dnE_{a,i,n} + mI_{a,i-1} - (\mu_a + \mu_I + r + m)I_{a,i}$$

Appendix 3.3S: Analysis of the DDE system.

We begin with a basic SEI model:

$$\begin{aligned}
\frac{\partial S}{\partial t} &= bN(1-N) - \mu S - \frac{\beta SI}{N} \\
\frac{\partial E}{\partial t} &= \frac{\beta SI}{N} - \mu E - kE \\
\frac{\partial I}{\partial t} &= kE - (\mu + \alpha + \rho)I
\end{aligned}$$

We introduce age structure by separating each group into age classes S_0,S_1,... where S_0 represents 0-1 year old devils and so on. We also add age-dependence in mortality (μ_a), fecundity (b_a) for devils in age class a, and disease transmission rates ($\beta_{(a1,a2)}$) representing rates of transmission from a devil of age a_1 to one of age a_2. Ageing is represented as an exponential decay function between age classes. The dummy variables a', i and j are used below for summation over age classes.

$$\begin{aligned}
\frac{\partial S_a}{\partial t} &= \sum_i b_i N_i (1 - \sum_j N_j) - \mu_a S_a - \frac{\sum_{a'} \beta_{(a',a)} I_{a'} S_a}{\sum_i N_i} + S_{a-1} - S_a \\
\frac{\partial E_a}{\partial t} &= \frac{\sum_{a'} \beta_{(a',a)} I_{a'} S_a}{\sum_i N_i} - \mu_a E_a - kE_a + E_{a-1} - E_a \\
\frac{\partial I_a}{\partial t} &= kE_a - (\mu_a + \alpha + \rho)I_a + I_{a-1} - I_a
\end{aligned}$$

To incorporate an exact latent period, we use a age- and time-continuous formulation of the dynamics, and then discretise it to create a set of Delay-Differential Equations. We use dummy variables a' and t' for integration over age and time respectively.

Let cohort $S(a,t)$ be the susceptible population born at time c, where $a(t) = t - c$ is a function of t:

$$\begin{aligned}\frac{dS(a,t)}{dt} &= -\mu(a)S(a,t) - \frac{\int_0^\infty \beta(a',a)I(a',t)da'}{N}S(a,t) \\ &= \left(-\mu(a) - \frac{\int_0^\infty \beta(a',a)I(a',t)da'}{N}\right)S(a,t) \\ &= -S(a,t)\frac{\partial R(a,t)}{\partial t}\end{aligned}$$

where $N = \int_0^\infty N(a',t)da'$ is the total population, and $R(a,t)$ is defined such that

$$\frac{\partial R}{\partial t} = -\mu(a) - \frac{\int_0^\infty \beta(a',a)I(a',t)da'}{N}$$

and by definition

$$\begin{aligned}\frac{\partial R}{\partial t} &= -\frac{1}{S}\frac{dS}{dt} \\ &= -\frac{d(\ln S)}{dt}\end{aligned}$$

so

$$\ln S(a,t) = \ln S(a-1,t-1) - \int_{t-1}^{t} \frac{\partial R(a-1,t')}{\partial t}dt'$$

and

$$S(a,t) = S(a-1,t-1)\exp\left(-\int_{t-1}^{t} \frac{\partial R(a-1,t')}{\partial t}dt'\right)$$

which gives us:

$$S(a,t) = S(a-1,t-1)\exp\Big(-(R(a-1,t) - R(a-1,t-1))\Big) \quad (1)$$

By the chain rule,

$$\begin{aligned}\frac{dS(a,t)}{dt} &= \frac{\partial S(a,t)}{\partial a}\frac{\partial a}{\partial t} + \frac{\partial S(a,t)}{\partial t} \\ &= \frac{\partial S(a,t)}{\partial a} + \frac{\partial S(a,t)}{\partial t}\end{aligned}$$

Let $S_a(t) = \int_a^{a+1} S(a',t)da'$ be the number of susceptible devils between the age of a and $a + 1$ at time t, where a is a non-negative integer.

Then

$$\begin{aligned}\frac{dS_a(t)}{dt} &= \int_a^{a+1} \frac{\partial S(a',t)}{\partial t} da' \\ &= \int_a^{a+1} \left(\frac{dS}{dt} - \frac{\partial S}{\partial a}\right) da' \\ &= -\int_a^{a+1} S(a',t)\frac{\partial R}{\partial t} da' - \int_a^{a+1} \frac{\partial S}{\partial a} da'\end{aligned}$$

At this point we require β and μ to be discrete functions, so let $\beta_{(a1,a2)} = \beta(a_1,a_2)$ and $\mu_a = \mu(a)$. This requirement implies that R is also a discrete function in a, and we can thus discretise R by letting $R_a(t) = R(a,t)$ where a is a non-negative integer.

$$= -\frac{dR_a}{dt}\int_a^{a+1} S(a',t)da' - [S]_a^{a+1}$$

and thus

$$\frac{dS_a(t)}{dt} = -S_a(t)\frac{dR_a}{dt} - (S(a+1,t) - S(a,t)) \tag{2}$$

Define $S_{a^-}(t)$ such that

$$\frac{dS_a^-(t)}{dt} = -S_a(t)\frac{\partial R_a}{\partial t} \tag{3}$$

and define $S_{a^+}(t)$ such that

$$\frac{dS_a^+(t)}{dt} = S(a,t) \tag{4}$$

so substituting from Equation 4 into Equation 1:

$$\frac{dS_a^+(t)}{dt} = \frac{dS_{a-1}^+(t-1)}{dt}\exp\Big(-(R_{a-1}(t) - R_{a-1}(t-1))\Big)$$

and combining Equations 2, 3 and 4:

$$S_a(t) = S_a^-(t) + S_a^+(t) - S_{a+1}^+(t)$$

Let cohort $E(a,t,l)$ be the exposed population born at time c, where $a(t) = t\text{-}c$ is a function of t, and having been exposed to the disease for time l starting at time l_0, where $l(t) = t - l_0$.

By the chain rule,

$$\frac{dE}{dt} = \frac{\partial E}{\partial t} + \frac{\partial E}{\partial a} + \frac{\partial E}{\partial l} = -\mu E$$

So

$$E(a + l, t + l, l) = E(a, t, 0)e^{-\mu l}$$

and thus

$$E(a + L, t + L, L) = E(a, t, 0)e^{-\mu L}$$

$$E(a, t) = \int_0^L E(a, t, l)dl$$

so

$$\begin{aligned}
\frac{\partial E(a,t)}{\partial t} &= \int_0^L \frac{\partial E(a,t,l)}{\partial t} dl \\
&= \int_0^L \left(\frac{dE}{dt} - \frac{\partial E}{\partial a} - \frac{\partial E}{\partial l} \right) dl \\
&= \int_0^L -\mu(a)E(a,t,l)dl - \int_0^L \frac{\partial E}{\partial a} dl - \int_0^L \frac{\partial E}{\partial l} dl \\
&= -\mu(a)E(a,t) - \int_0^L \frac{\partial E}{\partial a} dl - [E(a,t,L) - E(a,t,0)]
\end{aligned}$$

where we let $E(a,t) = \int_0^L E(a,t,l)dl$.

Now, let $E_a(t) = \int_a^{a+1} E(a',t)da'$. So

$$\begin{aligned}
\frac{dE_a(t)}{dt} &= \int_a^{a+1}\left(-\mu(a')E(a',t) - \int_0^L \frac{\partial E(a',t,l)}{\partial a}dl - [E(a',t,L) - E(a',t,0)]\right)da' \\
&= -\mu_a E_a(t) - \int_a^{a+1}\int_0^L \frac{\partial E(a',t,l)}{\partial a}dl\ da' - \int_a^{a+1}[E(a',t,L) - E(a',t,0)]da' \\
&= -\mu_a E_a(t) - \int_0^L \int_a^{a+1} \frac{\partial E(a',t,l)}{\partial a}da'\ dl - \int_a^{a+1}[E(a'-L,t-L,0)e^{-\mu L} - E(a',t,0)]da' \\
&= -\mu_a E_a(t) - \int_0^L \Big(E(a+1,t,l) - E(a,t,l)\Big)dl + \int_a^{a+1} E(a',t,0)da' \\
&\quad -e^{-\mu L}\int_a^{a+1} E(a'-L,t-L,0)da' \\
&= -\mu_a E_a(t) + E(a,t) - E(a+1,t) + \int_a^{a+1} E(a',t,0)da' - e^{-\mu L}\int_a^{a+1} E(a'-L,t-L,0)da'
\end{aligned}$$

Here we encounter a discretisation problem - $E(a\text{-}L, t\text{-}L, 0)$ is difficult to work with, especially if L is not rational. So we assume that animals do not age in the exposed period - not an entirely satisfactory assumption, but it makes the analysis much easier and is reasonable where $L << 1$. This means that $\partial E/\partial a = 0$ and $E(a'\text{-}L, t\text{-}L, 0) = E(a', t\text{-}L, 0)$, giving us

$$\frac{dE_a(t)}{dt} = -\mu_a E_a(t) + \int_a^{a+1} E(a',t,0)da' - e^{-\mu L}\int_a^{a+1} E(a',t-L,0)da'$$

If we define E_+ such that

$$\int_a^{a+1} E(a',t,0)da' = \frac{dE^+}{dt} = \frac{\int_0^\infty \beta(a',a)I(a',t)da'}{N}S(a,t)$$

then

$$\frac{dE_a(t)}{dt} = -\mu_a E_a(t) + \frac{dE^+(t)}{dt} - e^{-\mu L}\frac{dE^+(t-L)}{dt}$$

Let cohort $I(a,t)$ be the susceptible population born at time c, where $a(t) = t - c$ is a function of t, and

$$\frac{dI(a,t)}{dt} = -(\mu + \alpha + \rho)I(a,t)$$

We will make the assumption here that animals do not age when they become infectious - this is more reasonable in the case of DFTD, as the age-dependent mortality μ_a is dwarfed by the additional mortality from infection α. Additionally,

animals will generally die within a few months of the disease, leaving little time for ageing.

So

$$\frac{dI(a,t)}{dt} = -(\mu + \alpha + \rho)I(a,t) + E(a,t,L)$$

and

$$\frac{dI_a(t)}{dt} = -(\mu + \alpha + \rho)I_a(t) + e^{-\mu L}\frac{dE^+(t-L)}{dt}$$

The entire system can then be described by this set of equations:

$$S_a(t) = S_a^+(t) + S_{a+1}^-(t)$$

$$E_a(t) = E_a^+(t) + E_a^-(t)$$

$$N = S + E + I$$

$$\frac{dS_0^+(t)}{dt} = (1 - \sum_i N_i)\sum_i b_i N_i$$

$$\frac{dS_a^+(t)}{dt} = \frac{dS_{a-1}^+(t-1)}{dt}\exp\Big(-(R_{a-1}(t) - R_{a-1}(t-1))\Big)$$

$$\frac{dS^-}{dt} = -S\frac{dR}{dt}$$

$$\frac{dE^+}{dt} = \frac{\beta SI}{\sum_I N_i}$$

$$\frac{dE^-}{dt} = -\frac{dE^+(t-L)}{dt}e^{-\mu L} - \mu E$$

$$\frac{dI}{dt} = \frac{dE^+(t-L)}{dt}e^{-\mu L} - (\mu + \alpha + r)I$$

$$\frac{dR}{dt} = \mu + \frac{\beta I}{\sum_I N_i}$$

For $t < 1$,

$$\frac{dS_a^+(t)}{dt} = S_a(0)\exp\Big(-(R_{a-1}(t) - R_{a-1}(0))\Big)$$

For $t < L$,

$$\frac{dE^{-}}{dt} = -\frac{E_a(0)}{L}e^{-\mu L} - \mu E$$

$$\frac{dI}{dt} = -\frac{E_a(0)}{L}e^{-\mu L} - (\mu + \alpha + r)I$$

Appendix 3.4S: Discussion of life expectancy.

To gain an estimate of a devil's life expectancy, we used our estimates for fecundity and survival, and estimates from Jones et al. (2008) of the proportion of devils in various populations that are 3 years old or over.

We used a matrix model of the form:

$$\begin{bmatrix} 0 & f_1 & f_2 & f_3 & f_4 \\ s_0 & 0 & 0 & 0 & 0 \\ 0 & s_1 & 0 & 0 & 0 \\ 0 & 0 & s_2 & 0 & 0 \\ 0 & 0 & 0 & s_3 & s_4 \end{bmatrix}$$

where f_i is the fecundity of devils with age between i and i+1, and s_i the survival rate from age i to i+1. Any animals in the 4+ age class stay there until death.

Values from Lachish et al.(2007) were used for fecundity and survival; and, as in the main article, scaling factors for the fecundity were introduced directly, and survival rate was converted to mortality μ = - log(s). Mortality was then also given a scaling factor.

The eigenvalues and eigenvectors of this matrix were then calculated. The scaling factors were then modified such that:

- the dominant eigenvalue was equal to 1, signifying a stable distribution

and

- the dominant eigenvector, signifying the stable age distribution, contained a set proportion of 3+ year olds.

There is substantial variation in the proportion of 3+ year olds in Jones et al. (2008), though a value somewhere around 30% seems the most feasible (see Table 3.2S). However, this is by no means certain, and the natural life expectancy must remain somewhat in doubt.

A sensitivity analysis of life expectancy versus the required removal rates shows little difference within the range of potential values (see Fig. 3.1S). This is because the population's naïve growth rate is kept constant, so any increase in mortality is matched by an increase in fecundity. Any variations in results are due to the age-dependence in both of these values. Our value of 4 for life expectancy is thus kept in the absence of a more accurate analysis.

References

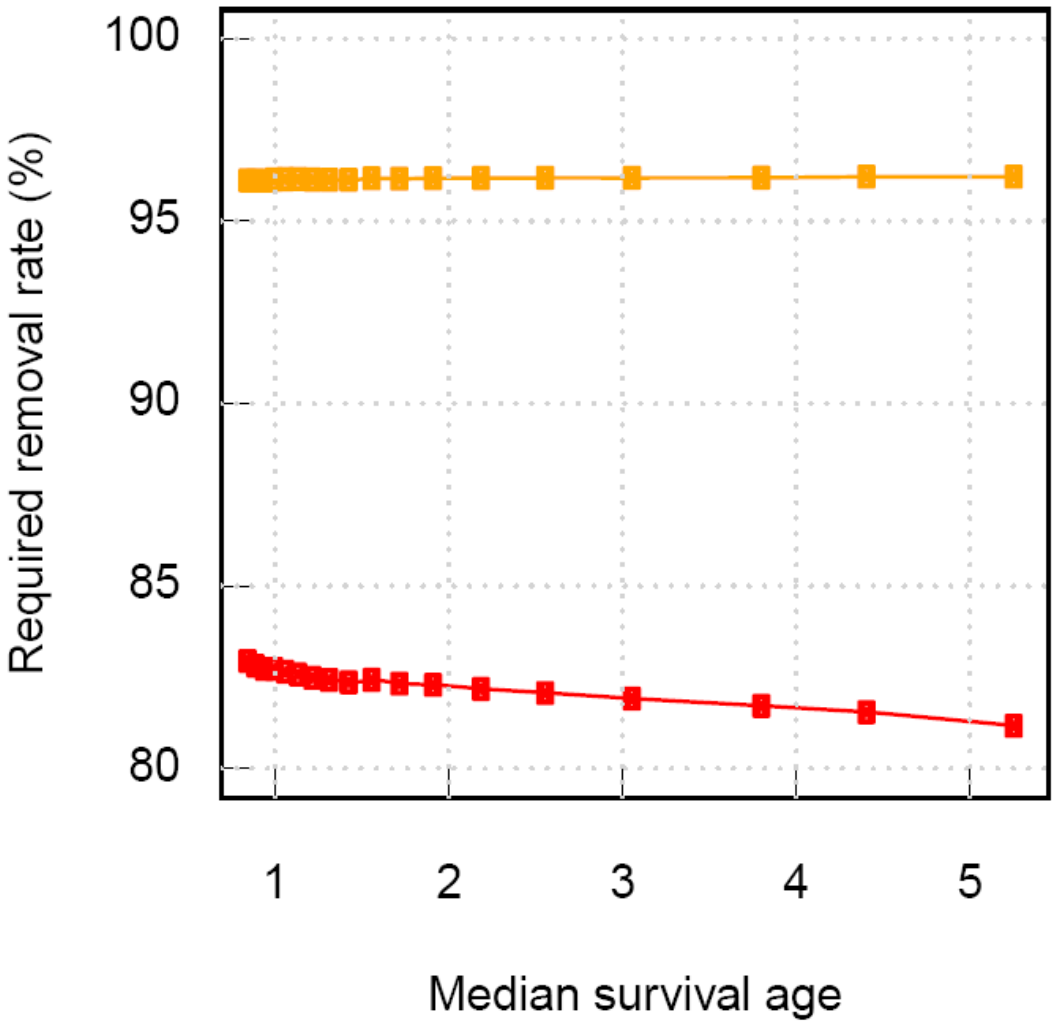
Jones, M. E., Cockburn, A., Hamede, R., Hawkins, C., Hesterman, H., Lachish, S., Mann, D., McCallum, H. & Pemberton, D. (2008) *Life history change in disease-ravaged Tasmanian devil populations*. *Proceedings of the National Academy of Science, USA* **105**:10023-10027.

Lachish, S., Jones, M. E. & McCallum, H. I. (2007) *The impact of devil facial tumour disease on the survival and population growth rate of the Tasmanian devil. Journal of Animal Ecology* **76**:926-936.

Table 3.2S: Proportion of 3+ year olds versus life expectancy.

Proportion of 3+ year olds	*Life expectancy (median age of death)*
20%	1.33
30%	1.90
40%	2.81
50%	4.11
60%	5.11

Figure 3.1S: Life expectancy versus required removal rates.



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Chapter 4. Estimation of modelling parameters using longitudinal data and
Bayesian MCMC analysis
(in preparation)

Chapter 5. Mapping the pre-disease Tasmanian devil population with limited
data
(in preparation)

Chapter 6. Spatial dynamics of Devil Facial Tumour Disease using reaction diffusion
modelling
(in preparation)

Chapter 7: General Discussion

“I'll forgive and forget
if you say you'll never go,
because it’s true what they say -
it's better the devil you know.”

- ***Kylie Minogue,*** **Better the Devil you Know**

Research summary

In this thesis, I have explored the epidemiology and effects of DFTD, as well as the effectiveness of disease management strategies. In this process, some novel techniques have been introduced which are generally applicable for use with wild species and associated infectious diseases. These objectives were achieved by using models covering multiple aspects of population and disease modelling. In particular, compartmental closed-population models, predictive regression statistical models, and spatial reaction-diffusion models have been developed.

First, I developed representative mechanistic models to simulate the effects of population-disease dynamics. These allowed me to predict the effect of artificially modifying dynamics, specifically by selectively culling infectious devils. Some parameters in these models were either uncertain or could be experimentally manipulated, so I analysed the potential effects of changing these parameters on dynamics, and used available data to generate parameter estimates empirically.

I then combined observation data with climate and vegetation predictors using a novel modelling technique to estimate the devil's natural abundance. I used this estimate to generalise the previously developed models into a novel spatial modelling framework. By combining this with data, I obtained best-fit estimates of disease spread and parameters.

This work has already helped to improve management strategies regarding the Tasmanian devil. In particular, I suggested in Chapter 3 that more regular removal would substantially improve the effectiveness of disease suppression, even with the

same overall level of effort. This suggestion was taken up by the Save the Tasmanian Devil Program for the trial on the Forestier Peninsula before it was deemed to be ineffective and cancelled in 2010. The modelling performed in Chapters 2 and 3 may also prove useful in later decisions concerning this currently unutilised management strategy.

Other findings of the study are also likely to have further direct and indirect impacts on management. Despite a dedicated and extensive research effort geared ultimately to saving the Tasmanian devil, there continue to be large gaps in knowledge. Unfortunately, the answers to some big questions – such as whether DFTD will inevitably bring about the devil's extinction in the wild, or whether a combination of effective management, genetic resistance and disease evolution may halt its spread – remain unknown and, despite our efforts, may be unknowable until the scenario resolves itself one way or another. However, much can be learnt through direct observation, experimentation, and - as is demonstrated in this thesis – through careful analysis of existing data.

In this discussion, I give some detail of how this thesis has contributed to answering important questions about devil-DFTD dynamics and management strategies, as well as along the way gaining information about population structure, devil habitats and introducing some new methods to solving these problems not only for the devil, but more generally in other wildlife diseases.

Applications for DFTD management

Haney and Power (1996) provide an example of an implementation of adaptive management as a step-by-step process:

- Define (or redefine) goals and objectives
- Model development (or revision) and hypothesis formation
- Prescription implementation
- Monitoring
- Model evaluation and data analysis

The process is repeated continually, updating the strategy with the newest available information. In their model, information exchange occurs throughout the process, meaning that up-to-date information is made available for all relevant parties at all times.

Direct applications

I have developed models that are particularly applicable in an adaptive management approach such as that described above. These models tested some hypotheses and current assumptions on the behaviour of the devil-DFTD system.

The findings of the models described in Chapter 3 indicated both that undergoing selective culling is currently unlikely to be effective, and that it may be worthwhile to find ways to make this strategy feasible in the future (see *Possible future directions*). Sensitivity analyses of model parameters demonstrated, however, that the difficulty of disease suppression for DFTD decreases with a decreasing latent period (see Fig 3.3), and alternatively, that a similar disease with a higher value for the latent period may not cause population extinction (as it would become infectious too late in its host's lifespan

– see Fig 2.1). These sensitivity analyses mean that the models' predictions could change if the latent period for DFTD were shown to be substantially different to current estimates.

To test these estimates, a Markov Chain Monte Carlo (MCMC) iterative process is used in Chapter 4 to fit the model to field data in order to test the current estimates of values for these model parameters. The results of this chapter suggest that the current estimates are reasonable based on current knowledge, but much uncertainty remains in the parameter estimates. More longitudinal data from diseased populations would be required to get an accurate handle on the model parameters.

Indirect applications

The modelling performed in the thesis also provides estimates of past or present information that can then be utilised in management actions. For example, in Chapter 5 a novel modelling technique is introduced that uses Boosted Regression Trees (De'ath 2007) to predict population abundance, takes both observation and model error into account, and uses both trap and spotlighting data to train the predictive model. The model's results give a much lower than expected estimate of devil abundance prior to the disease's emergence. As the proportional decline of the population can be estimated with some confidence based on spotlighting transect data (e.g. Hawkins et al. 2006), this result has direct conservation implications: the devil may already be in greater danger of succumbing to Allee effects than previously realised, meaning that extinction may be more likely and more sudden. In addition, a greater level of urgency may be needed in gathering captive breeding populations as less suitable devils may be available to recruit enough captive animals to repopulate the state, should it become necessary.

This kind of modelling can also suggest explanations for previously unexplained phenomena, point to future scenarios, and provide motivation for future work. To illustrate, though the Tasmanian devil's natural distribution is continuous, as it occupies the entire state (as demonstrated in Chapter 5), density of devil abundance is not uniformly abundant across the state. Most noticeably, the devil population appears to be of lower density in the south-west of the state. In addition, the results from Chapter 5 also suggest that a relatively narrow high-density area exists between the eastern and western populations of Tasmanian devil. This may help to explain the genetic variation that exists between these populations (Jones et al. 2004). It also suggests two reasons for the observed slowing of the spread of DFTD in this area (Hamede et al. 2011) – the existence of resistance to DFTD in the western population of devils, and/or the possibility of a relatively narrow corridor across which the disease can spread quickly.

An understanding of these phenomena is critical to be able to react appropriately to them. This is particularly important in the devil's case, as the slowing of the disease's spread can be used to advantage from a management perspective. This means that time still remains to isolate a wild disease-free population – at the time of writing, plans are being considered to fence off the Woolnorth property in the north western disease-free part of the state. It also means that adult disease-free devils can be taken from the disease free part of the state for insurance populations. This represents a substantial advantage, as the only devils that can be safely used from diseased parts of the state are juvenile devils and devils which have been quarantined for over a year. This length of time represents a large proportion of a devil's lifespan but is necessary to ensure that a

quarantined devil was not caught with latent disease, and will not compromise an insurance population.

In addition to this apparent slowing of the disease, questions were also raised about where DFTD emerged in Chapter 6. It has been assumed that it emerged in the far north-east of the state, but the simulation modelling suggested that it could just have easily emerged further south, and that this possibility should not be rejected without a more thorough investigation. This work could help to explain recent anomalies in DFTD detection such as the discovery of the disease in Zeehan in 2011, and could potentially be used to suggest future sites for devil monitoring.

Continuous monitoring of the spread of the disease is therefore vital in being able to pursue a flexible and adaptive management strategy. In Chapter 6, we presented a novel spatial modelling technique based on the dynamical system presented in Chapter 3, which is then fitted to monitoring data. We developed an approach which allowed the testing of assumptions about the spread of the disease such as the location of emergence, and whether the rate of spread of the disease is constant or slowing.

Wider applications of thesis methodology

Though the Tasmanian devil is unusual in many ways, and DFTD is certainly unique among threatening wildlife diseases, many of the techniques developed during the course of this thesis are widely applicable to other species. In particular, the use of multiple sources of data (Chapters 5 and 6) and the need to test models via dynamical systems analysis (Chapter 2), sensitivity analysis (Chapter 3) and parameter estimation (Chapter 4) are common ones in population dynamics and epidemiology. The present

study introduces some novel techniques and applications that can be more widely applied in these areas.

Selective culling

The effectiveness of culling for the control of animal diseases is currently a topic of debate in the scientific community. Using a "test-and-cull" or selective culling strategy has been shown to be logistically feasible for controlling chronic wasting disease in urban mule deer *Odocoileus hemionus* (Wolfe, Miller and Williams 2004) and modelling suggests that it may be effective in managing it in white-tailed deer *Odocoileus virginianus*, particularly if the disease has density dependent transmission (Wasserberg 2009). However, there are many cases in which culling strategies have proven ineffective and sometimes even counterproductive. Donnelly et al. (2003) reported that localised badger culling in reaction to bovine tuberculosis outbreaks actually appeared to increase disease prevalence in cattle, and Hallam & McCracken (2011) found that culling did not control white nose syndrome in bats for any of the modelled scenarios.

In Chapter 3, we contribute to the debate by modelling the potential effectiveness of a selective culling regime in controlling DFTD in Tasmanian devils. Our results confirm the conclusions of Lachish et al. (2010) that the disease suppression trial conducted in the Forestier peninsula from 2004-2010 would ultimately prove ineffective. We further demonstrated, similarly to Hallam & McCracken (2011), that it would also prove ineffective for all of our modelled scenarios without a currently infeasible level of suppression effort. As a result, to avoid inefficient use of available resources but also the possibility of making things worse, we recommended that culling should only be

attempted – either in trials, or on a full scale – once appropriate models have shown it is likely to be effective. In particular, diseases with a frequency dependent component such as DFTD are particularly unlikely to respond well to selective culling (e.g. Wasserberg et al. 2009). Our model provides a potential starting point for developing models to study other species where selective culling is being considered.

Population abundance

Abundance effects

Chapters 5 and 6 aimed to quantify population abundance, both in an unthreatened, stable, spatially contiguous population (Chapter 5) and in a dynamically changing population with its entire range threatened by disease (Chapter 6). The approach employed has wide ranging applications for other species, as the level of abundance in a wild animal population can affect its response to threats, such as infectious disease (Gulland 1995). As described in Chapter 1, many infectious diseases burn out when the density of a population is sufficiently low but others do not, and can pose an extinction threat. Low abundance can also in itself affect the population's general fitness via Allee effects (Stephens, Sutherland and Freckleton 1999). This is a particular risk for species with low genetic diversity (Newman and Pilson 1997), such as is the case with the Tasmanian devil. Understanding the overall abundance and localised population density of a species is therefore important for conservation, as populations that remain at a low level of abundance for extended periods, either locally or across their range, encounter an added host of risks.

Spatial aspects of population abundance

It is not only the size of a population that matters for conservation, but where individuals can be found. It is invaluable for conservation managers to know how the population of their species of interest is distributed across the landscape so as to more accurately assess the likely impact of a localised threat, or the spread of a disease to a new area. Habitat fragmentation can prove to be an additional risk for many species experiencing habitat loss by anthropogenic factors (Ewers and Didham 2006), climate change (e.g. coral reef fishes; Munday et al. 2008) or disease. Habitat fragmentation occurs when a species' distribution is broken apart into a number of smaller habitat fragments (Fahrig 2003). If species are unable to migrate between fragments with sufficient regularity, these less populous fragments can experience an increased level of extinction risk.

There is currently an opportunity for modellers to take advantage of relatively new and novel techniques to increase the accuracy of abundance and distribution predictions. Spatial modelling techniques are regularly used to find distributions of species (see Hirzel and Guisan 2002) and to estimate abundance based on spatial data (e.g. sambar deer *Cervus unicolour* in south-eastern Australia; Forsyth et al. 2009). However, many of these are based on relatively simplistic predictive techniques such as linear models, when a suite of more recently developed techniques are proving to be generally better predictors (Elith et al. 2006). These techniques are now becoming widely used for estimating species distribution, but have not so far been as well utilised for abundance estimation. Also, few models as yet account for observation error, though Royle et al. (2007) incorporated it into a novel hierarchical spatial model estimating abundance and occurrence maps of the European Jay *Garrulus glandarius*.

There is also scope for models to take better advantage of available sources of data. In many cases, multiple sources of information are available for estimating population abundance. Some of these sources act as indices for abundance, since they measure a trait of the species indirectly related to it: for example, Fernandez (2005) used pellets as an index for abundance of the European rabbit *Oryctolagus cuniculus* and VanDerWal et al. (2009) modelled spatial patterns of abundance using presence-only data.

The modelling framework developed in Chapter 5 uses Boosted Regression Trees (De'ath 2007) while dealing with multiple types of data and, as far as possible, incorporating model and observation error into its estimates. This work will hopefully provide a basis, or more general encouragement, for modellers working with other species to use data which may previously have been thought insufficient in quantity, quality or consistency for predictive modelling.

Spatial dynamics and abundance

Though deterministic spatial models have been used to model the spread of pathogens in controlled experiments (Dwyer 1992), less work has been done modelling the spread of wildlife diseases – instead, these tend to be modelled using stochastic algorithms (e.g. Smith et al. 2002). Deterministic models can provide a fast and efficient alternative where a qualitative estimate of dynamical behaviour is required. In Chapter 6 we use a deterministic reaction-diffusion system to model the spread of DFTD, fitting the model to field data provided by mark-recapture estimates of trapping data and spotlight transect data. Using both of these datasets together provided a more reasonable fit to the observed spread of the disease compared to using them individually, suggesting that

with sufficient data, such a model may be effective as a predictor of spatial spread. A reaction-diffusion framework can be coupled with a wide variety of model types, making it a robust technique usable in a range of epidemiological scenarios.

Possible future directions

It is almost impossible to predict a disease's effects on a population without first understanding the form of disease transmission (McCallum, Barlow and Hone 2001). In the case of the Tasmanian devil, a substantial body of evidence exists to suggest that DFTD transmission has a substantial frequency dependent component. Hamede, McCallum and Jones (2008) have suggested that biting during mating may represent a substantial proportion of disease infection. This in turn suggests that the disease may act like sexually transmitted diseases, which are generally frequency dependent (May and Anderson 1987). McCallum et al. (2009) demonstrated using an age-structured model that I provided (see Appendix I), that the results of mark-recapture studies are inconsistent with density dependent transmission, but are consistent with frequency dependent transmission.

The actual method of DFTD transmission may be slightly more complicated than this, however. Biting occurs primarily either during mating or during agonistic interactions over food. The existence of these two separate "modes" of transmission supports the hypothesis that disease transmission is some combination of frequency dependent and another functional form - most likely density dependent or similar. Appendix III provides another example of a study system where disease transmission was more complex than would intuitively be expected, especially considering the basic nature of the "ecological" system (in this case, simulated zombies and humans).

Developing a deeper understanding of how the disease is transmitted would be beneficial for future modelling work. It would lead to a greater level of predictive accuracy for modelling. In particular, it could remove potential confounding factors for parameter estimation. For example, models based on frequency dependent transmission alone may in some circumstances behave similarly to models incorporating multiple modes of transmission with higher disease infectiousness, but may behave very differently in other circumstances.

Deterministic dynamical models were found to be most effective in the present study for a number of reasons. The dynamics of the population-disease interaction are not fully understood, as demonstrated above. This means that models based on best estimates of dynamics are necessarily limited in their predictive ability. Deterministic models provide a reasonable estimate of the expected result of a host-disease interaction, with the notable exception of very low populations. In a system where confidence in modelling is limited to largely qualitative analysis, using deterministic models represents no noticeable sacrifice in accuracy. The gap in knowledge about dynamics means that exploration of the parameter space and of different modelling scenarios also becomes particularly necessary. This level of detailed exploration can prove to be prohibitive with stochastic models - they tend to be computationally intensive due to the need to run them repeatedly to encompass the range of stochastic dynamics.

Despite the difficulties in using stochastic models, they have a number of features that would make them an attractive target for future modelling work. Stochastic models are able to provide a probabilistic analysis of likelihoods of extinction, for example, which deterministic models are not able to handle. Such a model could determine an estimate

the level of risk of disease-caused extinction in pertinent scenarios. For Tasmanian devil management decisions, running these models could well be feasible on smaller-scale closed populations such as the Forestier and Freycinet Peninsulas, a fenced-off Woolnorth, or island populations such as that proposed for Maria Island (DPIPWE, unpublished data). Being more accurately able to estimate current modelling parameters would make stochastic modelling even more useful and allow more detailed analysis.

Though I demonstrated in Chapter 3 that disease suppression by selective culling is currently infeasible as a management tool, this may not always be the case. For example, it may become possible in the future to trap a larger proportion of the cryptic population, or the disease may be suppressed in some areas by the effects of genetic resistance. In these cases, selective culling may become an effective method either to speed the eradication of the disease or, less optimistically, to maintain a breeding population for longer.

The potential of a pre-clinical test for DFTD is currently being researched. If a test is successfully developed and becomes viable for field use, the test will be able to diagnose DFTD before tumours become visible – which is roughly the same point as when a devil with the disease becomes infectious. When, or if, it becomes available for use in the field, it could also add to the effectiveness of selective culling by removing infected devils before they have any chance to infect others. Its effectiveness in conjunction with selective culling, however, depends on its accuracy. The false positive rate (the proportion of results that return positive when the devil is DFTD-negative) and the false negative rate (the proportion of results that fail to detect DFTD where it is present) need to be sufficiently low for the test to be effective. The test also needs to

detect disease sufficiently early to detect enough devils which are infected but not yet infectious to suppress disease. Modelling work estimating the effects of a pre-clinical test on disease suppression efforts could provide thresholds below which a pre-clinical test could make disease suppression more feasible. Appendix II shows some preliminary modelling that could be refined in later work to give such an estimate.

Models rely on the availability of relevant data and information to make them valid and useful. Epidemiological models, like those described in this thesis, cannot be formulated without detailed knowledge about the system under study such as the mode of disease transmission, the effect on the disease on its host, and demographic information about the host. This experimental and observational data is often qualitative or tentative in its conclusions, but is vital to developing models on which hypotheses can be tested. In the case of the Tasmanian devil, field data from a study of social networks (Hamede, McCallum and Jones 2008) provided such competing hypotheses in regards to disease transmission. As a result of testing these hypotheses, the disease was shown to be inconsistent with density dependent transmission (McCallum et al. 2009). In turn, this information helped to define a reasonable mechanistic model (see Chapter 2) with which inferences could be made about dynamics (see Chapters 3, 4 and 6).

Information based on experimental or observational data could help to further improve models. In particular, the latent period of DFTD is currently not well known despite numerous cases of devils developing the disease in between trapping trips or in captivity. The primary problem in determining the latent period is that the transmission process – devils biting one another – is both logistically and ethically difficult to reproduce experimentally, and it is otherwise impossible to determine when infection

occurred. In addition, the latent period is likely to vary between devils due to a large number of variables affecting the progress of the disease in individual cases (Kate Swift, pers. comm.). However, developing techniques to analyse cases in which devils are observed before and after displaying symptoms of DFTD could result in better estimates of both the mean and spread of the disease's latent period. A surprising variety of data can form the basis of models that could provide information about the epidemiological process, and even data without an obvious immediate purpose is worth making available.

Epidemiological models cannot be tested without data with which to compare them and determine whether their behaviour genuinely describes the system under study. This data may come in the form of directly comparable data, for example abundance or prevalence estimates (used in Chapters 3-6), or indirectly comparable data such as indices to abundance like sightings during spotlighting surveys (used in Chapters 5-6). The more of this type of data that is available, the more power epidemiological and statistical models have to accurately describe the system. Long-term datasets are particularly desirable as they are capable of encompassing all stages of a disease's progress through the population (as used in Chapters 3, 5-6), but where this data is not available, indirectly comparable data, expert opinion or even anecdotal information can help to fill knowledge gaps.

Recent developments in statistical and mathematical modelling techniques, computing power, and epidemiological data collection – some of which have been described and exploited in this thesis – are allowing models to become more powerful predictors, and more flexible in dealing with new and different forms of information. As a result, the

increasing number of conservation issues that modelling is able to help address means that it is particularly well placed to contribute positively to wildlife conservation, both now and into the future.

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"This is not the end.
It is not even the beginning of the end.
But it is, perhaps, the end of the beginning."

- ***Sir Winston Churchill, 1942***

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Appendix II

I ran a quick model to estimate the effects of a preclinical test. I assumed that there are three important parameters that will affect the success of a removal trial:

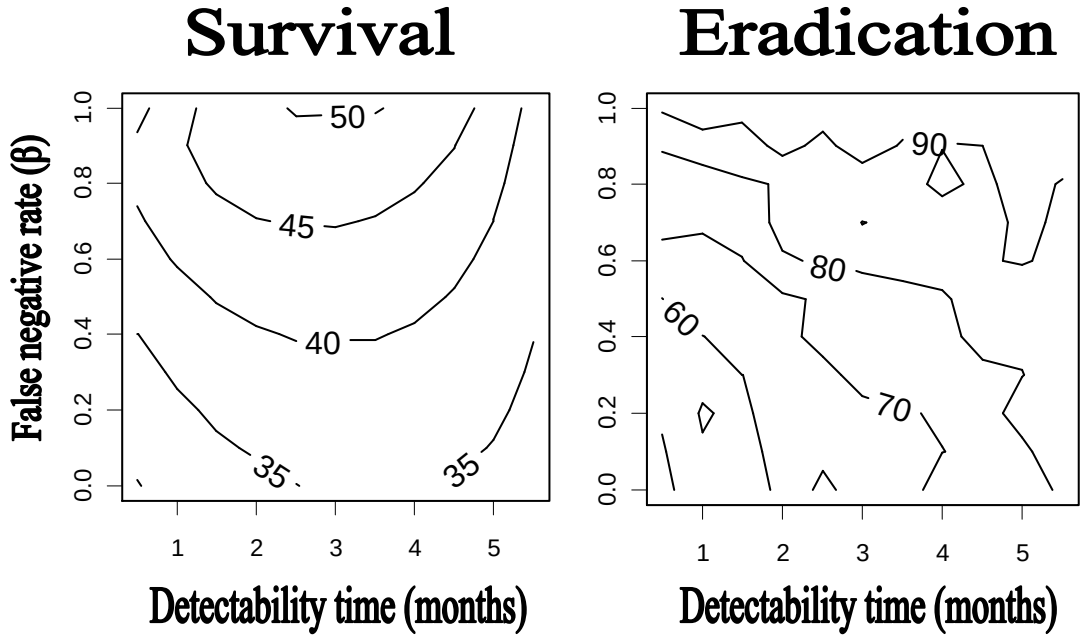
- The amount of time post-infection at which the disease is detectable by the pre-clinical test. We assume the latent period is 6 months here, so this time can vary between 0 (immediately effective) and 6 months (not useful).

- The false positive rate α – the proportion of positive DFTD test results that are incorrect (and are actually not diseased).

- The false negative rate β – the proportion of negative DFTD test results that are incorrect (and are actually diseased).

The most immediately obvious finding was that we require a VERY SMALL false positive rate for the test to be effective at all. The reason for that is that if we manage to trap a lot of devils, if we have a large false positive rate, we're removing a large quantity of healthy devils from the population and further suppressing the population we're trying to help! In the modelling I found that any false positive rate above 0.3% would not allow disease eradication no matter what the other parameters were set at. Of course, there are ways to ensure that this false positive rate of the testing process is sufficiently small: being cautious with the results and not necessarily rushing in to euthanase if a result is positive; perhaps running tests again; or even holding devils captive until their disease status is clearer.

The two contour plots below show the effects on required removal rate *(here measured in quarterly removal rate as a percentage, assuming continuous removal – a monthly trapping schedule should be a good approximation to this)* of varying the detectability window and the false negative rate, assuming that we have a perfect (0%) false positive rate. We notice that the rate required to keep the population alive is far lower than the rate required to eradicate disease. This may actually be a



problem with the model, as it doesn't agree with other numbers I have. I'm not sure, so we shouldn't assume that the required removal rate is really that low.

We notice that a detectability time around 3 months requires a higher removal rate for survival, though not for eradication. This is probably because removal can be a double-edged sword: while eliminating sources of infection, it also suppresses population numbers in the more immediate short term. So hence in cases where it's possible to eradicate the disease, this suppression won't make a substantial difference to the end result as the population is robust to some removal. However, in cases where management will struggle even to keep the population alive, the human-induced suppression can make a large difference (potentially even more so than this model indicates, due to stochastic effects).

To elaborate - for our survival contour plot, at the 6 months end of the spectrum the preclinical test is pointless and so will have no effect either way on the population. At 0 months, the test is effective on devils as soon as they are exposed to the disease, so will have maximum effect on disease; but on the negative side, will also suppress the population in the shorter term. However, around 3 months, the test is both suppressing devil populations and is only partially effective for disease suppression, and hence we see an increase in effort required to ensure survival. At least, this is why I think we're seeing these results!

For the eradication plot, we see a more expected result – the required removal rate increases both with the detectability time and the false negative rate. Assuming that β can be kept below about 0.2 (or 20%), it won't make a huge impact on the needed removal rate. The detectability time then becomes the most important parameter, and the required removal rate will decrease dramatically if the detectability time post-infection can be shortened.

From this very quick and dirty modelling, it appears that if false positives are eliminated from the preclinical test, and false negatives are limited, a detectability time of less than three months could make a successful eradication program much more feasible, though as mentioned care must be taken that the increase in removal associated with a preclinical test is not too much for an already weakened population.

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